Single dose application of cetrorelix in combination with clomiphene for friendly IVF: results of a feasibility study

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Abstract:

A prospective randomized feasibility study was carried out on 10 patients undergoing IVF treatment using a single-dose LHRH antagonist protocol (cetrorelix, Cetrotide®) with clomiphene citrate in combination with either human menopausal gonadotrophin (HMG) (n = 5) or recombinant human FSH (rFSH) (n = 5). Both treatment-groups, HMG and rFSH, were comparable with regard to age (33.2 ± 2.6 versus 34.4 ± 4.0 years) BMI (23.2 ± 2.6 versus 22.7 ± 1.6) and cause of infertility. They yielded comparable results concerning gonadotrophin dose (19.8 ± 8.7 versus 17.0 ± 8.9), stimulation days (6.5 ± 2.0 versus 5.8 ± 1.9) and live births (one versus two). No premature LH surge (LH >10 IU/ml and progesterone >1 ng/ml) occurred. The overall baby take-home rate was 30%. In a small number of patients, cetrorelix could be shown to effectively prevent premature LH surges in stimulation protocols combining clomiphene with gonadotrophins with an excellent baby take-home rate per started cycle of 30%.

References: 19 references open in new window

Articles that cite this article?

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Cetrorelix (Systemic)

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Description Return to top

Cetrorelix (set-RO-rel-lix) is a man-made hormone that blocks the effects of Gonadotropin Releasing Hormone (GnRH). GnRH controls another hormone that is called luteinizing hormone (LH), which is the hormone that starts ovulation during the menstrual cycle. When undergoing hormone treatment sometimes premature ovulation can occur, leading to eggs that are not ready for fertilization to be released. **Cetrorelix** does not allow the premature release of these eggs to occur.

This medicine is available only with your doctor's prescription, in the following dosage form:

Parenteral
- For injection (U.S.)

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In deciding to use a medicine, the risks of taking the medicine must be weighed against the good it will do. This is a decision you and your doctor will make. For **cetrorelix**, the following should be considered:

Allergies—Tell your health care professional if you have ever had any unusual or allergic reaction to **cetrorelix**, extrinsic peptide hormones (medicines similar to **cetrorelix**), mannitol, or any GnRH or GnRH-related medicines. Also tell your health care

professional if you are allergic to any other substances, such as foods, preservatives, or dyes.

Pregnancy—Cetrorelix is not recommended during pregnancy. Before taking this medicine, make sure your doctor knows if you are pregnant, or may become pregnant.

Breast-feeding—It is not known whether **cetrorelix** passes into the breast milk. However, it is not recommended during breast-feeding because it may cause unwanted effect in nursing babies.

Older adults—Cetrorelix is not intended for use in patients over the age of 65 years.

Other medical problems—The presence of other medical problems may affect the use of **cetrorelix**. Make sure you tell your doctor if you have any other medical problems, especially:

- Kidney disease—May increase your chance of side effects from **cetrorelix**.

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Take this medicine only as directed by your doctor. If you are to begin on Day 5, count the first day of your menstrual period as Day 1. Beginning on Day 5, take the correct dose every day for as many days as your doctor ordered. To help you to remember to take your dose of medicine, take it at the same time every day.

- Read the paper with information for the patient carefully.
- Understand and use the proper method of safely preparing the medicine.
- Wash your hands with soap and water and use a clean work area to prepare your injection.
- Make sure you clearly understand and carefully follow your doctor's instructions on how to give yourself an injection, including using the proper needle and syringe. Remember to change the site of injection to different areas to prevent skin problems from developing.
- Throw away needles, syringes, bottles, and unused medicine after the injection in a safe manner.

*Tell your doctor when you use the last dose of **cetrorelix*** . **Cetrorelix** often requires that another hormone called human chorionic gonadotropin (hCG) be given as a single dose the day after the last dose of **cetrorelix** is given. Your doctor will give you this medicine or arrange for you to get this medicine at the right time.

Dosing—

The dose of **cetrorelix** may be different for different patients. *If you are receiving **cetrorelix** at home, follow your doctor's orders or the directions on the label.* The following information includes only the average doses of **cetrorelix**. *If your dose is different, do not change it* unless your doctor tells you to do so.

- For *injection* dosage form:
  - For treatment of female infertility:
    - Adults—3 milligrams (mg) injected under the skin one time on Day 7 of your menstrual cycle, or 0.25 mg injected under the skin starting on Day 5 or 6 of your menstrual cycle and continuing until HCG administration occurs.

Missed dose—

If you miss a dose of this medicine, discuss with your doctor when you should receive your next dose. Do not double doses. If you have any questions about this, check with your doctor.

Storage—

To store this medicine:

- Keep out of the reach of children.
- Keep the packaged tray in the outer carton to protect it from light.

- Do not store in the bathroom, near the kitchen sink, or in other damp places. Heat or moisture may cause the medicine to break down.
- Store the 0.25 mg vials in the refrigerator , keep from freezing.
- Store the 3 mg vials at room temperature.

Precautions While Using This Medicine Return to top

It is very important that your doctor check you using ultrasound examination at regular visits to make sure that you are ready for injection with another drug (HCG) to induce ovulation.

Call your doctor immediately if you have taken more of the medication than your doctor ordered..

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Side Effects of This Medicine

Along with its needed effects, a medicine may cause some unwanted effects. Although not all of these side effects may occur, if they do occur they may need medical attention.

Check with your doctor immediately if any of the following side effects occur:

- *Less common*
  - Abdominal or stomach pain; continuing or severe nausea, vomiting or diarrhea; decreased amount of urine; feeling of indigestion; moderate to severe bloating; pelvic pain, severe ; rapid weight gain; shortness of breath; swelling of lower legs

Other side effects may occur that usually do not need medical attention. These side effects may go away during treatment as your body adjusts to the medicine. However, check with your doctor if any of the following side effects continue or are bothersome.

- *More common*
  - Headache; injection site bruising, itching, swelling, or redness; nausea

Other side effects not listed above may also occur in some patients. If you notice any other effects, check with your doctor.

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In the U.S.—

- Cetrotide

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- **Infertility**

Developed: 11/03/2000
Revised: 06/22/2004

billings LIFE WOOMB World Organisation Ovulation Method Billings

Fertility Disorders and the Billings Ovulation Method

Dr. Pilar Vigil P. Faculty of Biological Sciences Pontifical Catholic University of Chile

This paper was presented at the International Jubilee Conference, 50th Anniversary of Billings Method, UNiversity of Melbourne, Australia, conducted by Ovulation Method Research & Reference Centre of Australia, March 28-30, 2003.

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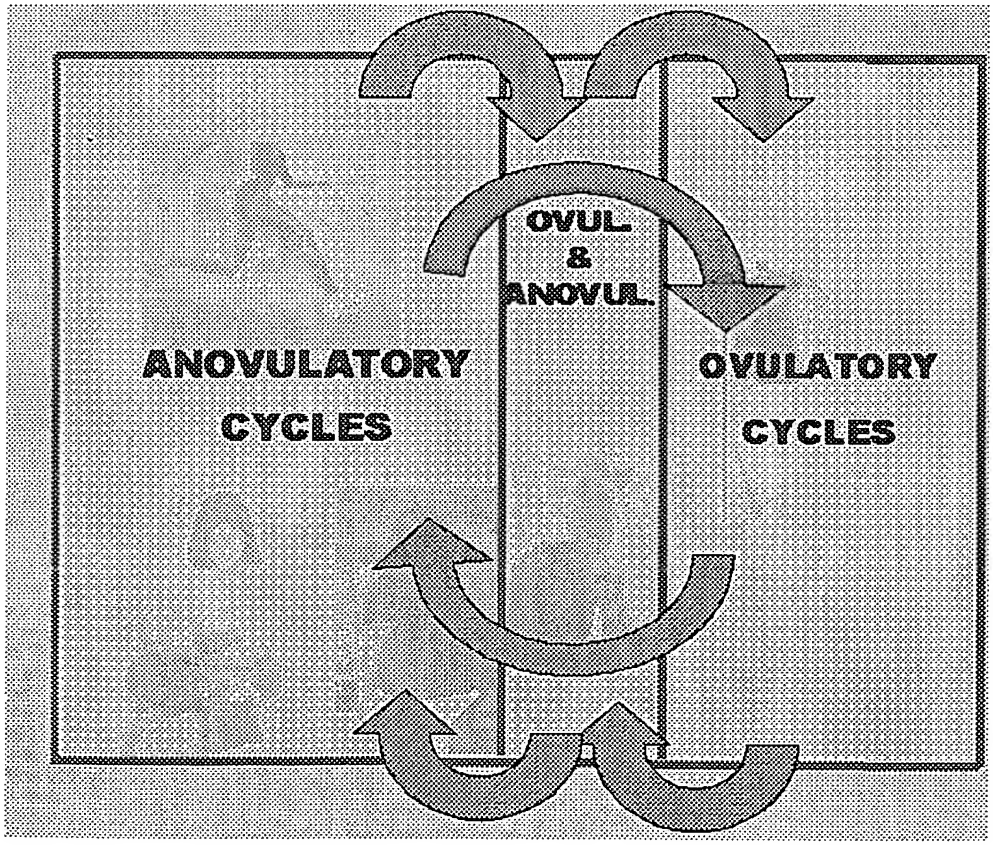
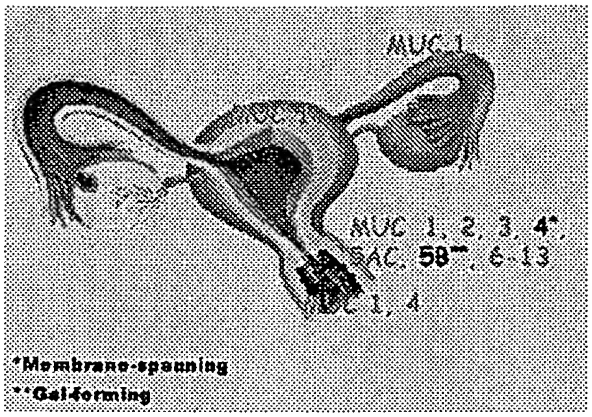
Introduction

Fertility is a transient biological state that depends on the fertility potential of the couple. During a women's lifetime, the ovary will go through different states of hormonal secretion and ovulation. The concept of the ovarian cycle as a continuum considers that all types of ovarian activity encountered during the reproductive life are normal responses to different environmental conditions in order to ensure the health of the mother and child.

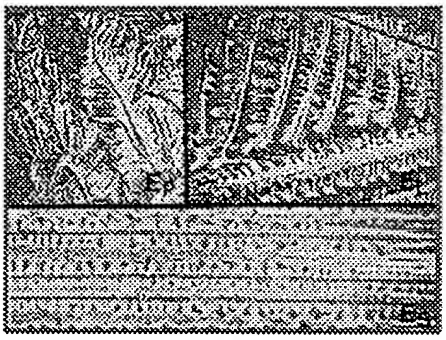
During the first two years after menarche, occasional anovulatory cycles may occur. However, subsequently, a healthy ovary will exhibit regular monthly ovulations, characterized by a 25 to 36 day cycle (32, 33, and 35). The ovulatory cycles are normally only interrupted by pregnancies and breastfeeding. Normal ovulatory activity and fertility are restored following pregnancy and breast feeding, however, stress or excessive exercise may result in a chronic ovulatory dysfunction that requires therapy. Anovulatory cycles frequently occur as menopause approaches. This is an expected part of woman's reproductive life cycle.



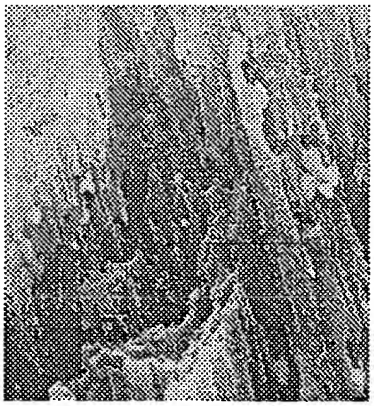
The use of the ovarian monitor has made it possible to identify hormonal variations during different periods of a woman's life and to correlate these changes with the mucus patterns (5, 6, 7). Thousands of measurements have been recorded for this purpose around the world, including Chile. These investigations have raised an enormous amount of information (24, 24). The amount and type of mucus secreted by the cervix changes through the ovarian cycle in response to fluctuating hormonal levels (26, 30 and 31). Mucins are the main components of mucus (18). To date a total of 13 distinct mucin genes have been identified (11,18). Mucins are categorized into 3 groups on the basis of their structural properties: membrane spanning (MUCs 1, 3, 4, 12 and 13, gel forming (MUCs 2, 5AC, 5B and 6) and small soluble (MUC 7). The four large gel-forming mucin genes are located on chromosome 11.p15.5 (12,18). Mucin 5B is the major gel forming mucin expressed by the endocervical epithelium and its expression peaks at midcycle (10). Message levels for mucin 4 also peak at midcycle. Two main types of cervical mucus have been described: oestrogenic and progestative. According to O'deblad's model, the oestrogenic type can be subdivided in L, S and P subtypes (4). The L subtype is the most abundant type of mucus during the periovulatory period and the P subtype appears close to ovulation (8). Message for all mucins diminishes as progesterone levels increase in blood. (11) During the luteal phase the progestative type of mucus is present.

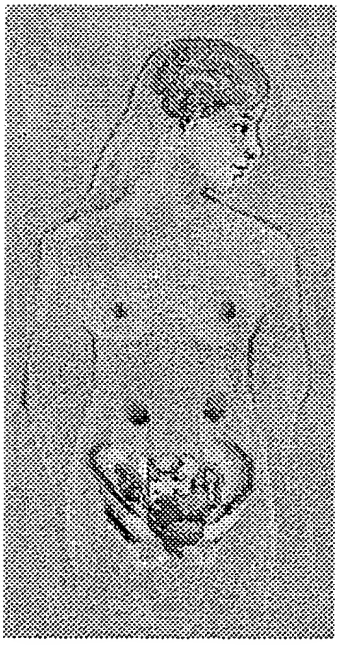


Estrogenic types of mucus: EP, ES, EL



G mucus, stimulated by Progesterone





The usefulness of the BOM in helping women to identify the different stages of her reproductive life cycle has been clearly demonstrated (3 , 4). The BOM is an invaluable tool in helping women to identify these conditions through fertility awareness. As Drs. Billings have stated "self awareness of fertility and infertility is an important knowledge which should be available to every woman. The woman who knows her own mucus patterns will be able to detect a number of gynecological disorders".

Questions arise as to when irregularities within the mucus patterns and the menstrual cycle should be considered abnormal and when is the point when a woman should be sufficiently concerned to consult a physician.

The persistence of such factors may increase a woman's risk of other reproductive system disorders and may be due to serious metabolic or endocrine abnormalities or to other diseases all of which need to be recognized.

Menstrual disorders and alteration in the mucus pattern can be caused by obstetrical, endocrine, gynecologic or iatrogenic disorders. Early pregnancy complications such as metrorrhagia and vaginal spotting should be identified by recognizing a previous fertile phase with a peak day and can be ruled out with the use of ultra sensitive pregnancy tests and pelvic ultrasound.

Ferility Disorders

Numerous studies have shown that 10 -15% of couples suffer with a fertility disorder. These are mainly due to: a) ovulatory dysfunction (OD) generally caused by hormonal disorders and b) inflammatory processes usually secondary to genital tract infections (GTI), mainly sexually transmitted diseases.

Ovulatory dysfunction is the most common disorder diagnosed in infertile couples (37%) and is predominantly associated with irregular menstrual cycles (IC). Irregular cycles are present in 10% of women, but having an irregular cycle doesn't necessary mean having an ovulatory dysfunction. We have been able to show according to the BOM charting that 43% of women with irregular cycles present an ovulatory dysfunction, which can be characterized by the absence of ovulation or abnormal ovulatory activity, as seen in cycles with short or abnormal luteal phases. On the other hand, young nuliparous women with regular cycles, (i.e., cycle length between 25 and 36 days) may also present an ovulatory dysfunction as identified by BOM charts (32).

Ovulatory Dysfunctions

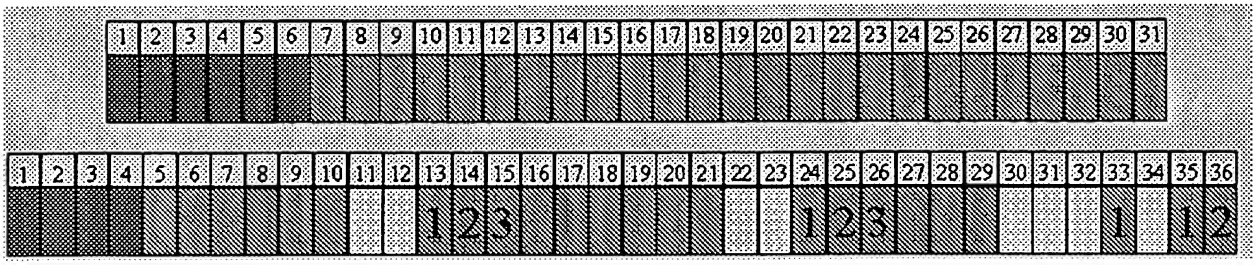
Endocrinological disorders

Endocrinological disorders are the most common cause of ovulatory dysfunction (27, 28, and 32). They can be divided into hypothalamic disorders, pituitary disorders, general endocrine disorders and adrenal and/or ovarian disorders (1).

Hypothalamic disorders

Hypothalamic disorders (e.g., anorexia nervosa) are characterized by hypo-estrogenic cycles with the persistence of "dry" days. Amenorrhea may be present. This type of cycle is also seen in athletes, although in this case it should be considered as a normal part of the continuum. In the later case there is a frequent return to regular ovarian cyclic activity as observed within three months of less strenuous physical exercise. However, some of the young women in this category may further develop an anorectic state and despite discontinuation of strenuous physical activity they do not return to normal cycles.

Hypoestrogenic cycles: Anorexia athletes

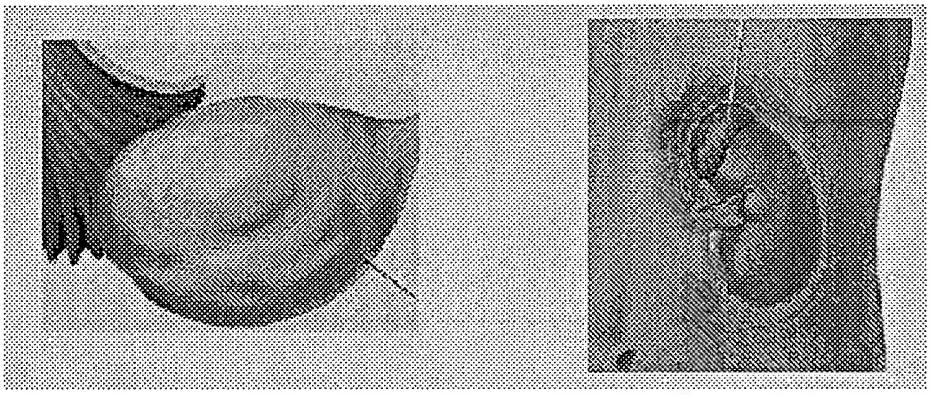


Endocrinological disorders (cont'd)

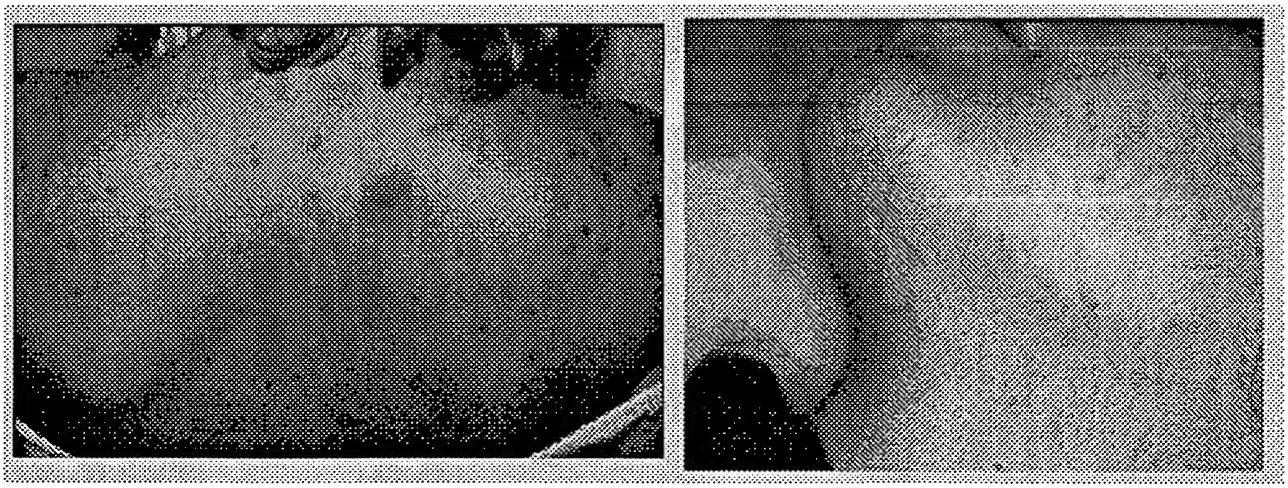
Ovarian-Adrenal dysfunctions

Adrenal and ovarian abnormalities are the most frequent cause of ovarian dysfunctions. The most common is the polycystic ovarian syndrome: an ovulatory dysfunction caused by hyperandrogenemia. In these women, irregular cycles are usually present, early after menarche (21, 22, 28).

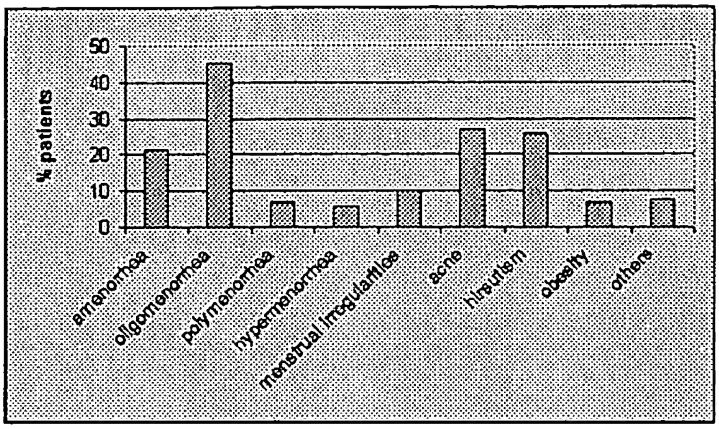
Polycystic Ovarian Syndrome(PCO)



They can also complain because of acne and/or hirsutism as well as increased body weight and mood changes.



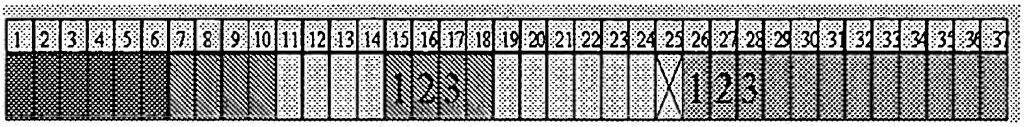
Reasons for consulting a physician in women with PCO (number of patients = 229, more than one reason for some patients)



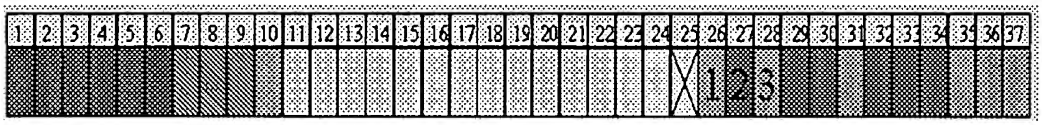
Cycles are characterized by a hyper estrogenic state where a continuous fertile type of mucus pattern is identified or mucus patches are present. Cycles can be ovulatory, with a long follicular phase or anovulatory.

Hyperestrogenic cycles

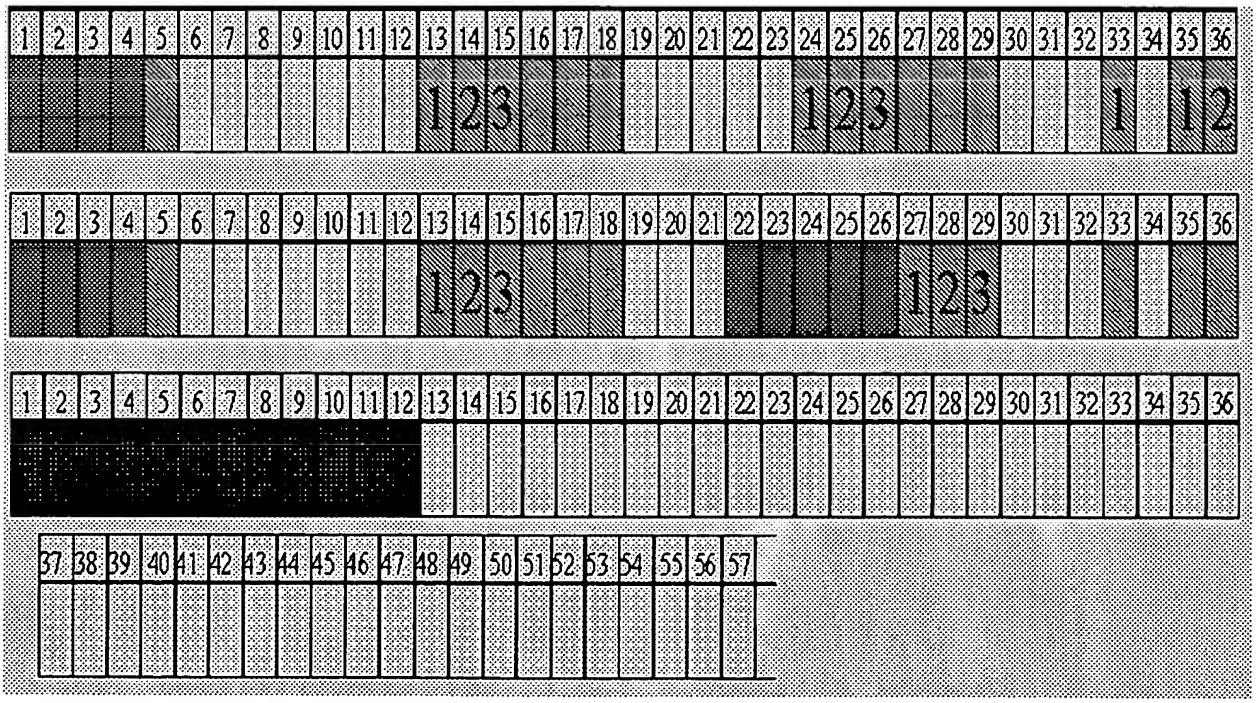
Doubtful peak



Long follicular phase

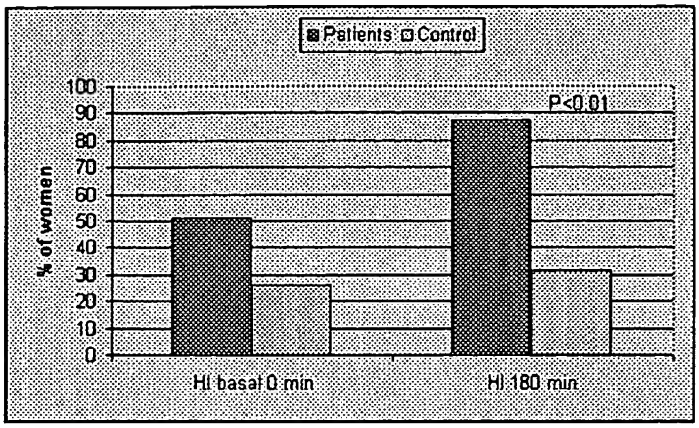


Anovulatory cycles



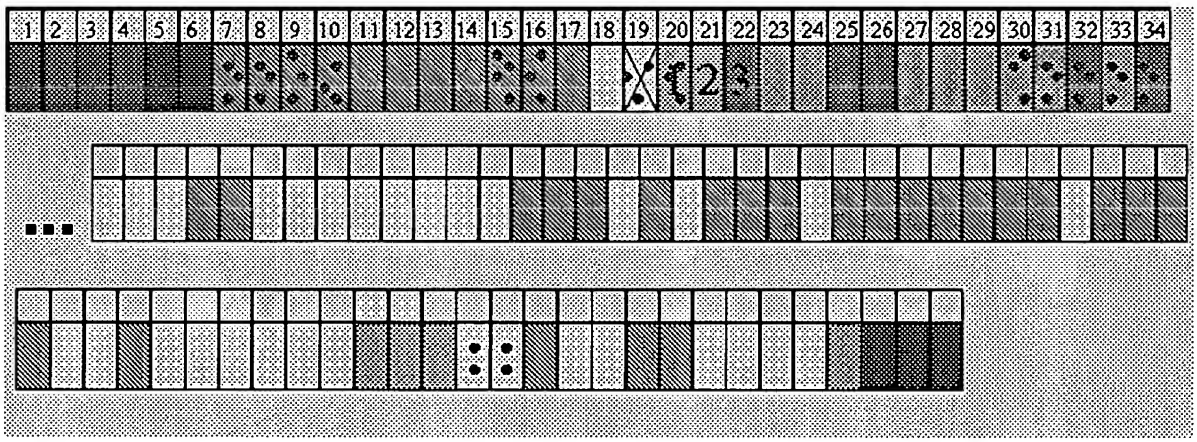
When a young woman complains because of menstrual abnormalities, the teaching of self-awareness of fertility in order to identify ovulatory dysfunctions is very important in order to be able to rule out metabolic conditions such as hyper insulinemia. Our studies have shown that in 86% of women who present with menstrual irregularities, an endocrine abnormality is present of which hyperandrogenemia is the most common (80% of cases (32). It is important to note that an impaired insulin response to oral glucose tolerance test is a commonly (80% of time) associated condition in these women (36). This requires treatment to prevent the occurrence of type II diabetes mellitus (22). Proper care, including diet, exercise and medical treatment will restore normal cyclical ovarian activity. Women who know how to recognize their mucus symptoms will be able to follow the improvement of their endocrine abnormality.

Abnormal insulin response to oral glucose tolerance test in PCO patients as compared to normal women at 0 and 180 minutes (number of women = 94)



Hypothyroidism is a less frequent (about 2%) (32) cause of ovarian dysfunction but it and hyperthyroidism, have to be considered. Different types of ovarian dysfunction can be observed in patients with thyroid disorders. Menorrhagia (15) is frequently associated to hypothyroidism. Although there is no specific pattern of ovarian activity associated to these endocrine abnormalities they should always be kept in mind and eliminated as a possible cause.

Menorrhagia



Women with ovulatory dysfunctions associated to irregular cycles and abnormal mucus patterns will not usually resume normal cycling spontaneously without appropriate treatment. Follow up studies have shown that in the absence of treatment these conditions only worsen with time (22, 23).

Other conditions, such as premature ovarian failure may also be a cause of fertility disorders presenting with irregular mucus patterns in response to fluctuating estrogen levels. These conditions are also observed in the perimenopausal period, where some cycles show an ovulatory pattern. As the condition worsens, anovulatory cycles will predominate.

In fertile women, naturally occurring midcycle cervical mucus studied with scanning electron microscopy, shows an arrangement of parallel fibers oriented along the main axis of the mucus sample, probably corresponding to the S subtype (2). Sperm transport maybe facilitated by this normally occurring condition. At midcycle, cervical mucus is greater in quantity, has more mucin and less protein and has higher water content than in the luteal phase (19). This increase in the amount of mucin in the cervical canal, because of its hydrophilic character, probably functions to retain or hold water in place at the cell surface, keeping in this way the cervical canal patent for sperm migration. Also this increase in mucin at a period of high water content could help in the protection of the cervix. Pathogens or other toxins may be trapped by the mucin thus preventing their entry into the uterus and Fallopian tubes (12). Future research is needed to establish mucus ultra structure and biochemical properties under different endocrinological abnormalities. Also, the function of the specific mucins and mucus types remains to be determined as well as their possible alterations.

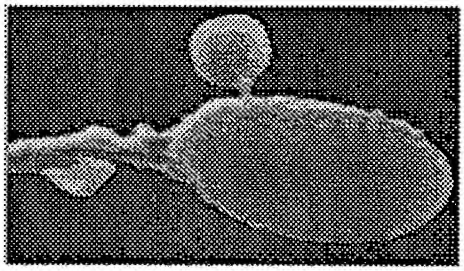
Gynecologic Disorders

Genital Tract Infections

Menstrual disorders and alteration in the mucus pattern can also be caused by gynecologic disorders such as anatomical abnormalities, neoplasia or inflammatory diseases.

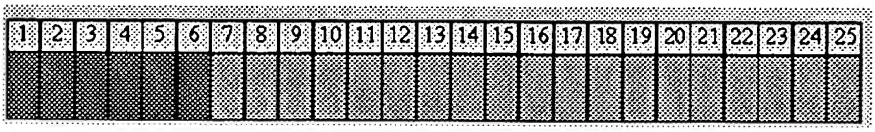
The second most frequent cause of fertility disorders are inflammatory processes, usually secondary to genital tract infections (GTI), which predominantly have an origin in sexually transmitted diseases. Microbial mucin degrading enzymes are associated with sexually transmitted infections and produced by the offending micro organisms. These enzymes will alter the mutually beneficial cohabitation that normally exists between commensals such as Lactobacillus, which use glycogen as an energy source and contribute to normal mucin turnover by the production of mucin degrading enzymes such as sialidase. Mucin molecules would be partly or completely degraded by the microbial enzymes. These molecules dictate the rheological properties which determine the amount and viscosity of the mucus, so these properties will change in response to enzymes produced by microbial organisms in the genital tract (37).

Human spermatozoa from infected male patient with Ct



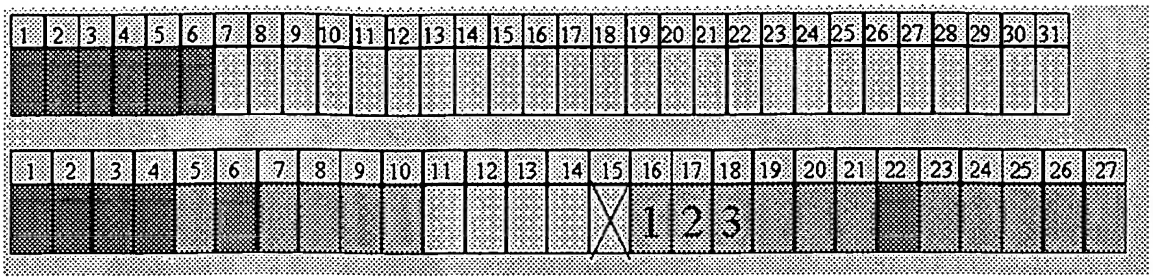
A woman who knows her own mucus pattern in times of health will be able to early recognize a GTI. These will usually cause a continuous discharge whose characteristics will depend upon the etiologic agent causing the infection. In general, an ovulatory pattern is identifiable, but it is associated with a creamy, sticky BIP. Symptomatic infections (itching and a characteristic discharge) are usually caused by fungi, bacteria or parasites. Chlamydia trachomatis infections, with an incidence of 13% in infertile couples and often associated with tubal pathology, (30, 34) will be asymptomatic or present with continuous moistness and variable degrees of pelvic pain. This infection may also show a mucopurulent discharge associated with the mucus discharge. The recognition of this infection and timely treatment may prevent fertility disorders.

Continuous discharge: Symptomatic infections caused by fungi, bacteria

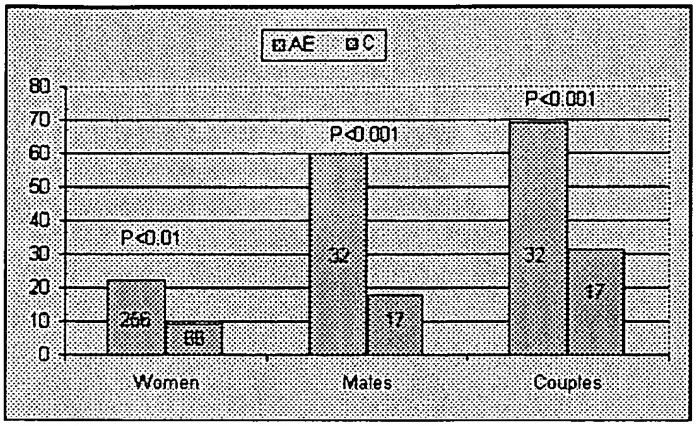


It has been shown that these infections provoke pelvic inflammatory processes and are associated with spontaneous abortions. Recent studies (20) have shown that the mesh spacing between mucin fibers is large enough for small viruses as human papiloma virus (HPV), associated to cervical neoplasia, to diffuse unhindered through mucus. Bacterial vaginosis related bacteria, micoplasms, trichomonas vaginalis, and gardnerella among others, must also be considered when unusual mucus patterns or menstrual irregularities occur. In this situation, both members of the couple should be treated in order to restore the healthy condition.

Continuous discharge: Symptomatic infections caused by virus(HPV), Chlamydia



Incidence of Chlamydia trachomatis in groups of males females and couples with or without first trimester spontaneous abortions



Contraceptive Pill

Fertility disorders may also be iatrogenic, caused by contraceptive pills or by hormonal therapy. Women coming off the pill may present cycles with short luteal phases, absence of a well defined mucus pattern, indicating anovulation, (21) poor mucus response due to damaged cervical epithelium and a poor menstrual flow due to alterations of the endometrial lining. Major cycle disturbances lasting for up to seven cycles (cycle length > 35 days or luteal phase of < 10 days, monophasic basal body temperature or anovulatory cycles) occur frequently in women, after discontinuation of the birth control pills. It has also been shown that in comparison with formerly used mechanical anti-conception methods; pill users have lower monthly percentages of conception during the first three months and a somewhat lower percentage between the fourth and tenth months after discontinuation of the pill (13, 14, and 16).

Conclusion

Self knowledge acquired by learning the BOM is an invaluable tool for women willing to achieve a healthy reproductive system state. Thus, identification of medical and environmental causes of abnormal menstrual cycle patterns may provide clues to the causes of the most frequent fertility disorders. Early diagnosis of these alterations, as can be achieved through self fertility awareness, will not only improve fertility disorders, but may help in the diagnosis and treatment of other pathologies such as metabolic conditions, endocrine disorders, anatomical alterations, pelvic inflammatory diseases or even neoplasia. Moreover, the menstrual cycle pattern should be taken into consideration in the clinical decision-making process.

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Day : Monday
Date: 8/21/2006
Time: 15:32:51

PALM INTRANET

Inventor Information for 10/661780

Inventor Name	City	State/Country
BOUCHARD, PHILIPPE	PARIS	FRANCE
FRYDMAN, RENE	PARIS	FRANCE
DEVROEY, PAUL	AALST	BELGIUM
DIEDRICH, KLAUS	GROSS SARAU	GERMANY
ENGEL, JURGEN	ALZENAU	GERMANY

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fertility LifeLines

Fertility LifeLines™ is open Monday-Friday: 8AM-midnight ET. Saturday-Sunday: 8AM-6PM ET.

Cetrotide®

Cetrotide® (cetrorelix acetate for injection

FAQ's

What is Cetrotide®?
What is the LH Surge and how does it affect **infertility**?
How does Cetrotide® prevent the LH surge?
When should I use Cetrotide®?
Which dosing regimen of Cetrotide® should I choose?
How is Cetrotide® administered?
Who should not use Cetrotide®?
Are there any side effects associated with the use of Cetrotide®?
Where can I get more information about Cetrotide®?
How long can I keep Cetrotide® after it has been reconstituted?

What is Cetrotide®?top ^

Cetrotide® is an injectable drug that controls hormonal responses in your body, which can affe the development of eggs in your ovaries. Specifically, Cetrotide® helps to prevent a hormonal event known as the "LH surge."

What is the LH Surge and how does it affect infertility?to ^

The LH Surge is a natural hormonal response that signals the release of a mature egg from an ovary. While undergoing **infertility** treatment, if an LH surge occurs too early in a cycle, eggs a released before they can fully mature. This greatly reduces the opportunity to retrieve the eggs later use in Assisted Reproductive Technologies (ART). The LH surge is caused by a series of changes involving two hormones — gonadotropin — releasing hormone (GnRH) and luteinizing hormone (LH). When GnRH is present, it triggers a dramatic rise, or "surge," in LH levels.

How does Cetrotide® prevent the LH surge?top ^

Cetrotide® works by directly blocking the trigger effect of GnRH. This blocking action stops a possible LH surge before it begins, allowing eggs to reach the level of development needed for fertilization. Because of the way it works, Cetrotide® is called a GnRH antagonist.

When should I use Cetrotide®?top ^

You only need to use Cetrotide® for the short part of your cycle in which an LH surge is a conc This is the part of your cycle when your eggs are nearing maturity.

Which dosing regimen of Cetrotide® should I choose?top

Cetrotide® is available in two dosing regimens — a single dose (3 mg), which controls the LH surge for up to 4 days, or a daily dose (0.25 mg) given over a short period of time. Your healthcare provider has chosen the regimen that best meets your individual needs. Be sure to follow your healthcare provider's specific instructions for dose strength and schedule.

How is Cetrotide® administered?top ^

Cetrotide® is given as a subcutaneous (under the skin) injection.

Who should not use Cetrotide®?top ^

You should not use Cetrotide® if you answer "yes" to any of the following questions. If you are unsure if you should use Cetrotide®, talk with your healthcare provider.

- Do you have a known allergy to **cetrorelix** acetate, GnRH or any other GnRH analogs, exogenous peptide hormones or mannitol?
- Are you pregnant or do you suspect you may be pregnant?
- Are you currently breast-feeding?
- Do you have severe renal impairment?

Are there any side effects associated with the use of Cetrotide®?top ^

You should review with your Fertility Specialist the risks and benefits of using Cetrotide®. As w any medication, report any and all side effects, symptoms or physical changes to your healthca provider.

Cetrotide® can cause serious side effects including ovarian hyperstimulation syndrome (OHSS) and lung and blood vessel problems.

Pregnancy loss (miscarriage) is higher in women receiving fertility drugs than in women not tak fertility drugs.

Because it acts quickly and directly, Cetrotide® is generally well tolerated. The most common s effects include mild and short-lasting reactions, like reddening, itching, and swelling, may occu the injection site. Some patients also experience nausea and headaches. For complete product details, see the Full Prescribing Information.

Where can I get more information about Cetrotide®?top

If you have any questions, be sure to contact your Fertility Specialist for more information or guidance. You can also call Serono Fertility LifeLines™ toll-free at 1-866-LETS-TRY (1-866-53 7879).

How long can I keep Cetrotide® after it has been reconstituted?top ^

The solution should be used immediately after preparation.

If you have any additional questions, be sure to contact your Fertility Specialist for more information or guidance. You can also call Fertility LifeLines™ toll-free at 1-866-LETS-TRY (1-8 538-7879). All calls are free and confidential.

Full Prescribing Information for Cetrotide® (**cetrorelix** acetate for injection) (195 KB)

Looking for definitions for fertility terms? Visit our Glossary.

Fertility LifeLines™
1-866-LETS-TRY (1-866-538-7879)

Monday - Friday: 8am - midnight ET; Saturday and Sunday: 8am - 6pm ET

1: J Med Chem. 1994 Mar 4;37(5):701-5.

In vitro and in vivo activities of reduced-size antagonists of luteinizing hormone-releasing hormone.

Haviv F, Fitzpatrick TD, Nichols CJ, Bush EN, Diaz G, Bammert G, Nguyen AT, Johnson ES, Knittle J, Greer J.

TAP Pharmaceuticals, Inc., Abbott Park, Illinois.

A novel series of octapeptide LHRH antagonists was designed on the basis of the structure of the (2-9) fragment of a LHRH agonist. By adopting a systematic SAR study, we were able to improve first the in vitro activity and then the in vivo LH suppression, raising them up to the range of the decapeptide antagonists NalGlu (51) and A-75998 (50), resulting in A-76154 (49). The octapeptide antagonist A-76154 is the most potent reduced-size LHRH antagonist reported. It suppresses LH in the castrated rat by over 80% for a period of 4 h following sc bolus administration of 30 micrograms/kg.

PMID: 7510341 [PubMed - indexed for MEDLINE]

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 NEWS  8  MAY 30   IPC 8 Rolled-up Core codes added to CA/CAplus and
                   USPATFULL/USPAT2
 NEWS  9  MAY 30   The F-Term thesaurus is now available in CA/CAplus
 NEWS 10  JUN 02   The first reclassification of IPC codes now complete in
                   INPADOC
 NEWS 11  JUN 26   TULSA/TULSA2 reloaded and enhanced with new search and
                   and display fields
 NEWS 12  JUN 28   Price changes in full-text patent databases EPFULL and PCTFULL
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 NEWS 16  AUG 09   INSPEC enhanced with 1898-1968 archive

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=> s cetrorelix
L1 4 CETRORELIX

=> d 1-4

L1 ANSWER 1 OF 4 REGISTRY COPYRIGHT 2006 ACS on STN
RN 896710-47-7 REGISTRY
ED Entered STN: 28 Jul 2006
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phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-L-tyrosyl-N5-(aminocarbonyl)-
D-ornithyl-L-leucyl-L-arginyl-L-prolyl-, monohexadecanoate (9CI) (CA
INDEX NAME)
OTHER NAMES:
CN Cetrorelix palmitate
FS PROTEIN SEQUENCE; STEREOSEARCH
MF C70 H92 Cl N17 O14 . C16 H32 O2
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER

RELATED SEQUENCES AVAILABLE WITH SEQLINK

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CMF C70 H92 Cl N17 O14

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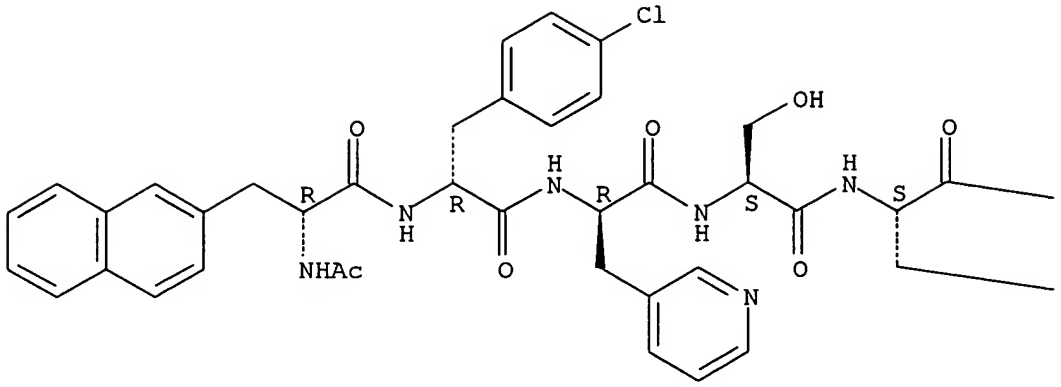

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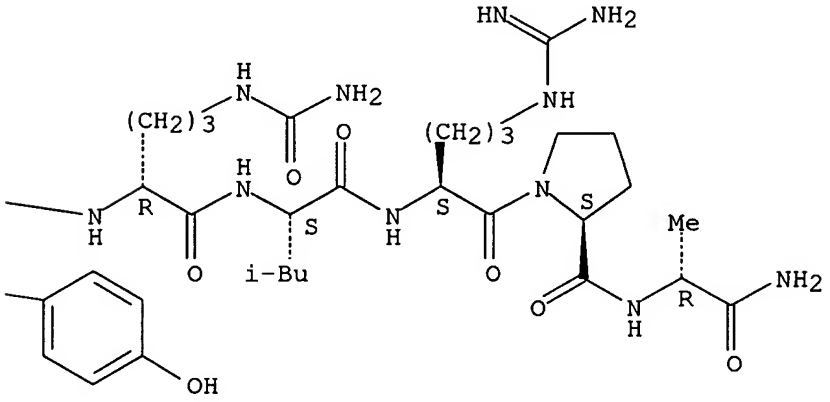

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L1 ANSWER 2 OF 4 REGISTRY COPYRIGHT 2006 ACS on STN
RN 165186-69-6 REGISTRY
ED Entered STN: 25 Jul 1995
CN D-Alaninamide, N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-D-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-L-tyrosyl-N5-(aminocarbonyl)-D-ornithyl-L-leucyl-L-arginyl-L-prolyl-, 4,4'-methylenebis[3-hydroxy-2-naphthalenecarboxylate] (2:1) (salt) (9CI) (CA INDEX NAME)
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CN 2-Naphthalenecarboxylic acid, 4,4'-methylenebis[3-hydroxy-, compd. with N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-D-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-L-tyrosyl-N5-(aminocarbonyl)-D-ornithyl-L-leucyl-L-arginyl-L-prolyl-D-alaninamide (1:2) (9CI)
OTHER NAMES:

CN Cetrorelix embonate
FS PROTEIN SEQUENCE; STEREOSEARCH
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SR CA
LC STN Files: CA, CAPLUS, IMSPATENTS, IMSRESEARCH, TOXCENTER, USPAT2, USPATFULL

RELATED SEQUENCES AVAILABLE WITH SEQLINK

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CRN 120287-85-6
CMF C70 H92 Cl N17 O14

RELATED SEQUENCES AVAILABLE WITH SEQLINK

Absolute stereochemistry.

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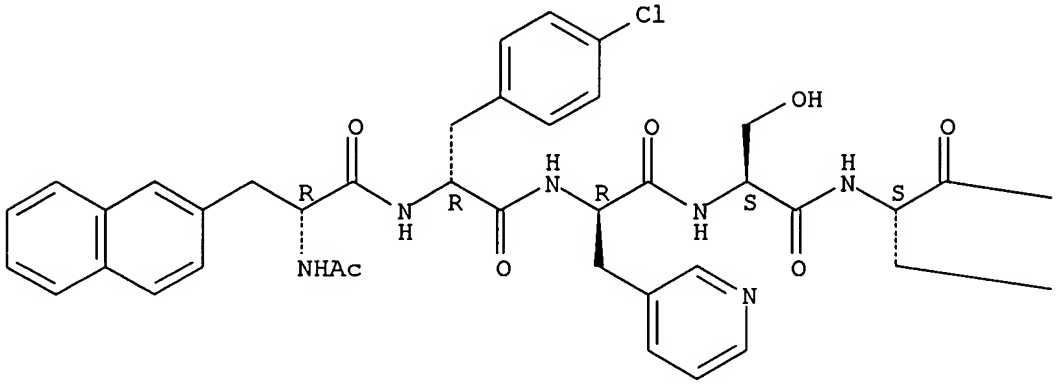

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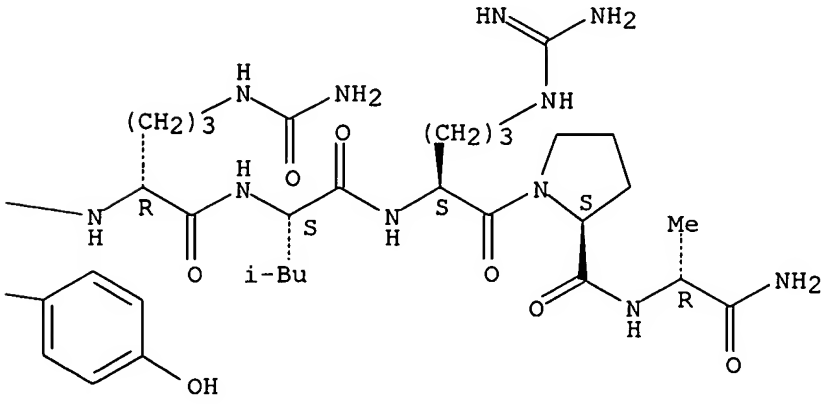

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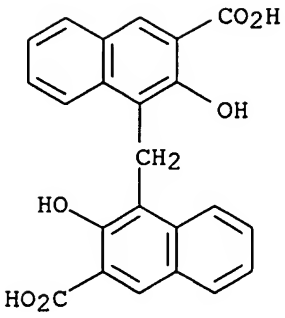

5 REFERENCES IN FILE CA (1907 TO DATE)
5 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L1 ANSWER 3 OF 4 REGISTRY COPYRIGHT 2006 ACS on STN
RN 145672-81-7 REGISTRY
ED Entered STN: 03 Feb 1993
CN D-Alaninamide, N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-D-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-L-tyrosyl-N5-(aminocarbonyl)-D-ornithyl-L-leucyl-L-arginyl-L-prolyl-, acetate (salt) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Cetrorelix acetate
CN Cetrotid
CN Cetrotide
CN D 20761
CN NS 75A
CN SB 075 acetate
FS PROTEIN SEQUENCE; STEREOSEARCH
MF C70 H92 Cl N17 O14 . x C2 H4 O2
SR CA
LC STN Files: BIOSIS, CA, CAPLUS, CIN, IMSPATENTS, IMSRESEARCH, IPA, MRCK*, PATDPASPC, PS, TOXCENTER, USAN, USPAT2, USPATFULL
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RELATED SEQUENCES AVAILABLE WITH SEQLINK

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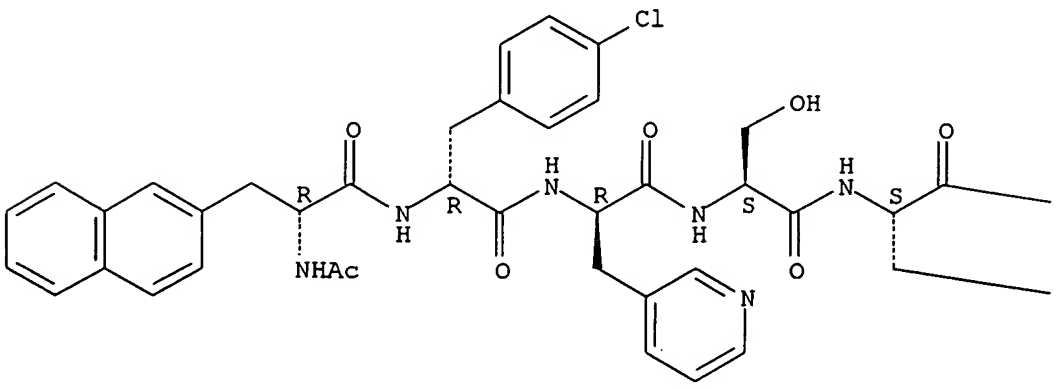

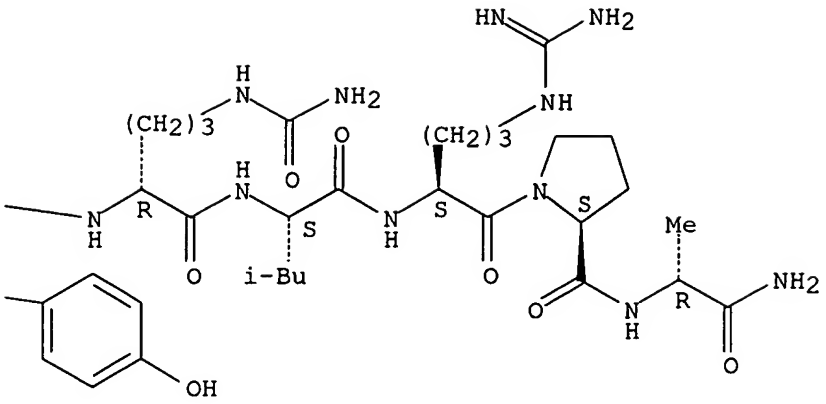

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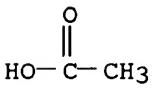

81 REFERENCES IN FILE CA (1907 TO DATE)
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L1 ANSWER 4 OF 4 REGISTRY COPYRIGHT 2006 ACS on STN
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OTHER NAMES:
CN 3: PN: WO0018423 PAGE: 26 claimed protein
CN Cetrorelix
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CI COM
SR CA
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Absolute stereochemistry.

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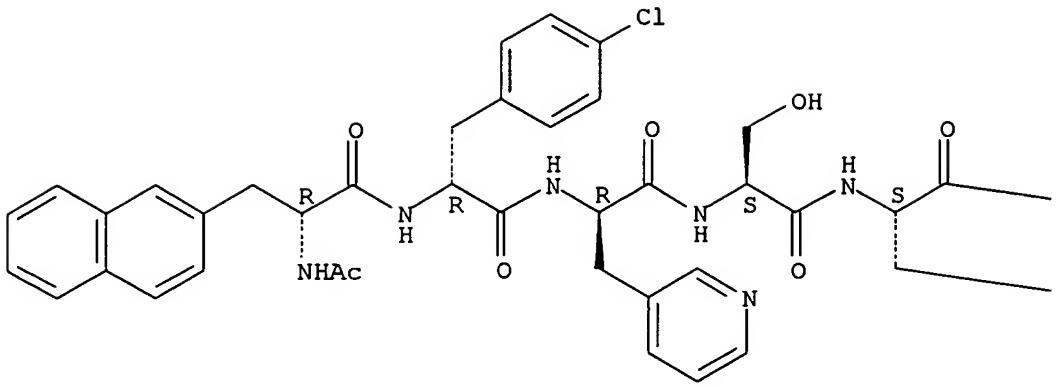

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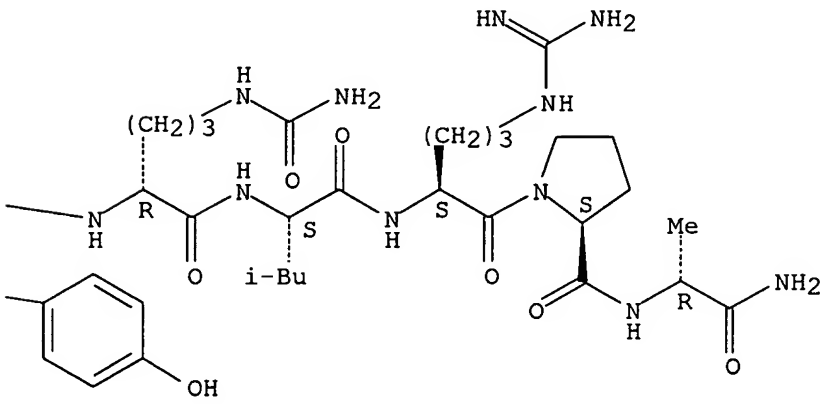

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

305 REFERENCES IN FILE CA (1907 TO DATE)
7 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
306 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> s ganirelix or anatarelix antide or azaline b or ramorelix or a 76154 or nal-glu or 88-88

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             6 88-88
                 (88(W)88)
L2          12 GANIRELIX OR ANATARELIX ANTIDE OR AZALINE B OR RAMORELIX OR A
               76154 OR NAL-GLU OR 88-88

=> d 1-12

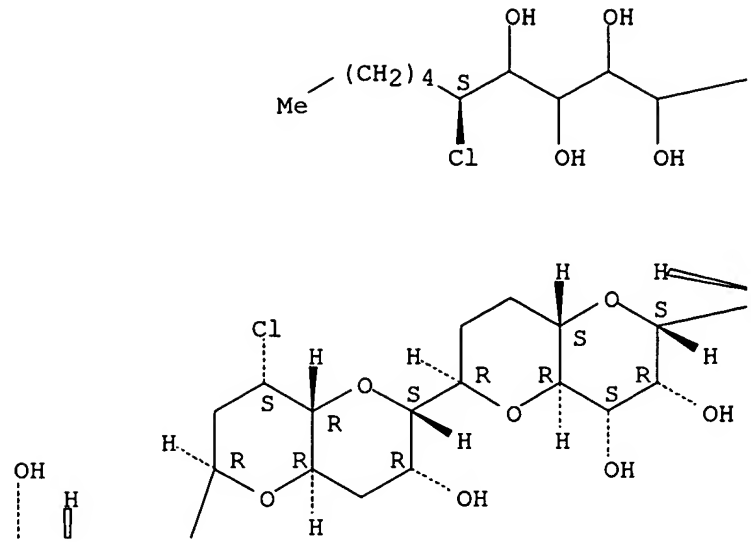
L2   ANSWER 1 OF 12  REGISTRY  COPYRIGHT 2006 ACS on STN
RN   288259-78-9  REGISTRY
ED   Entered STN:  06 Sep 2000
CN   Nal-Glu ORF 21234 (9CI)  (CA INDEX NAME)
ENTE A LHRH antagonist
MF   Unspecified
CI   MAN
SR   CA
LC   STN Files:   CA, CAPLUS

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
               1 REFERENCES IN FILE CA (1907 TO DATE)
               1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

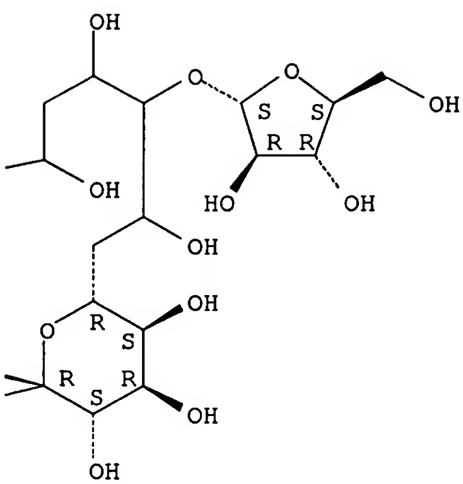
L2   ANSWER 2 OF 12  REGISTRY  COPYRIGHT 2006 ACS on STN
RN   221381-62-0  REGISTRY
ED   Entered STN:  21 Apr 1999
CN   Prymnesin 2, 1-dechloro-1,2,3,3,4,4,7,7,8,8,9,10,11,12,16,17,18,19,87
     ,87,88,88,89,89,90,90-hexacosahydro- (9CI)  (CA INDEX NAME)
OTHER NAMES:
CN   1-Dechloroperhydroprymnesin 2
FS   STEREOSEARCH
MF   C96 H163 Cl2 N O35
SR   CA
LC   STN Files:   CA, CAPLUS, CASREACT, TOXCENTER

Absolute stereochemistry.
Currently available stereo shown.
```

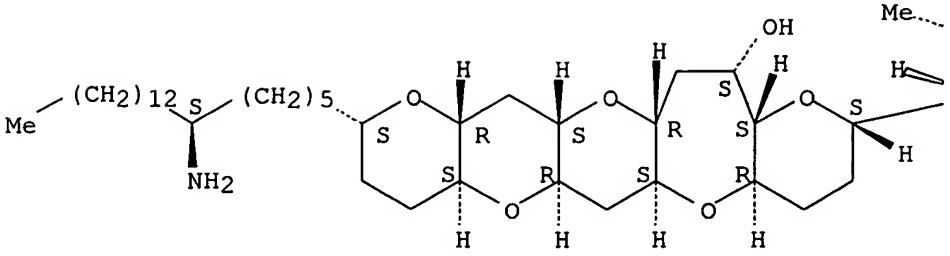
PAGE 1-B



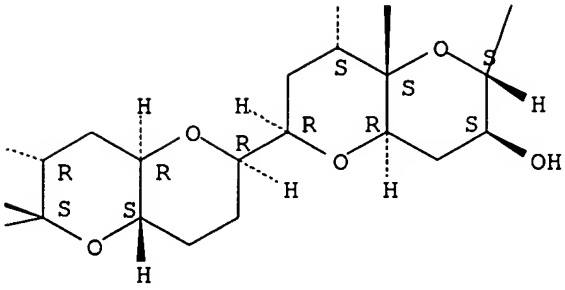
PAGE 1-C



PAGE 2-A



PAGE 2-B



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L2 ANSWER 3 OF 12 REGISTRY COPYRIGHT 2006 ACS on STN
RN 168849-75-0 REGISTRY
ED Entered STN: 13 Oct 1995
CN 79,101-(Methanoxy[1,4]benzenomethano[1,4]benzenoxymethano)-9,12:14,17:47,50:52,55-tetraetheno-27,31:71,75-dimethano-41,61-(methanoxy[1,4]benzenomethano[1,4]benzenoxymethano)-2,66:3,65:23,37:24,36-tetrametheno-1H,7H,13H,19H,25H,33H,35H,45H,51H,57H,67H,69H-bis[1,3]benzodioxocino[9,8-d:9',8'-d']bis[1,3]benzodioxocino[9',10':24,25;10'',9'':39,40][1,3,7,17,21,23,27,37], octaoxacyclotetracontino[4,5-j:20,19-j']bis[1,3]benzodioxocin, 1,25,33,35,67,69,77,103-octapentyl-13,13,51,51,88,88,116,116-octakis(trifluoromethyl)-, stereoisomer (9CI) (CA INDEX NAME)
MF C172 H168 F24 O24
SR CA
LC STN Files: CA, CAPLUS, CASREACT

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

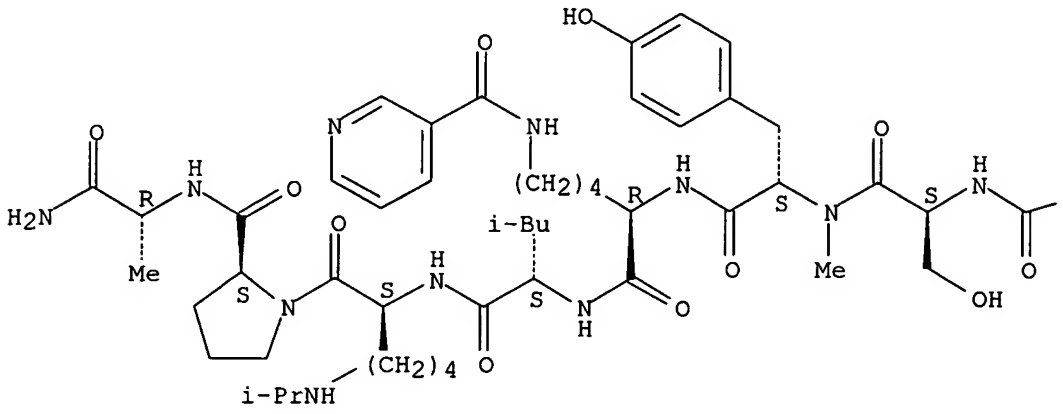
L2 ANSWER 4 OF 12 REGISTRY COPYRIGHT 2006 ACS on STN
RN 136989-30-5 REGISTRY
ED Entered STN: 01 Nov 1991
CN D-Alaninamide, N-[3-(4-fluorophenyl)-1-oxopropyl]-3-(1-naphthalenyl)-D-alanyl-L-seryl-N-methyl-L-tyrosyl-N6-(3-pyridinylcarbonyl)-D-lysyl-L-leucyl-N6-(1-methylethyl)-L-lysyl-L-prolyl- (9CI) (CA INDEX NAME)

OTHER NAMES:
CN A 76154
FS PROTEIN SEQUENCE; STEREOSEARCH
MF C70 H93 F N12 O12
CI COM
SR CA
LC STN Files: CA, CAPLUS, IMSRESEARCH, MEDLINE, PROUSDDR, TOXCENTER

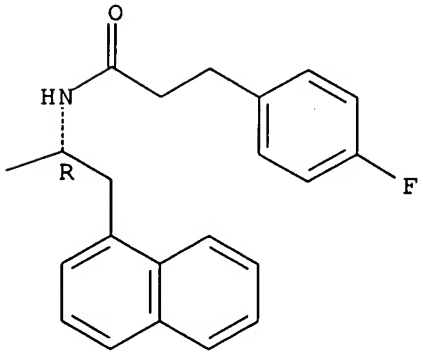
RELATED SEQUENCES AVAILABLE WITH SEQLINK

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



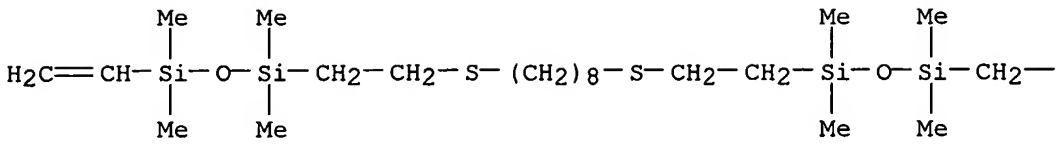
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

3 REFERENCES IN FILE CA (1907 TO DATE)
3 REFERENCES IN FILE CAPLUS (1907 TO DATE)

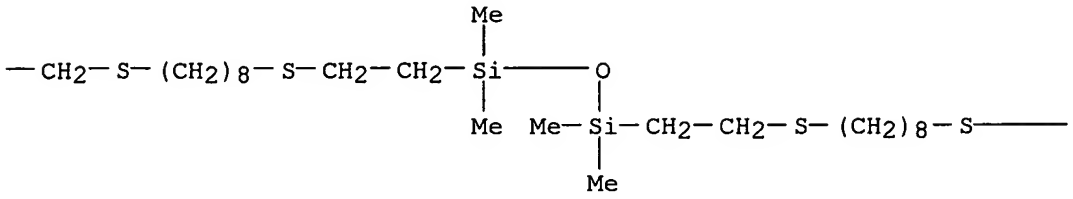
L2 ANSWER 5 OF 12 REGISTRY COPYRIGHT 2006 ACS on STN
RN 134798-68-8 REGISTRY
ED Entered STN: 12 Jul 1991
CN 4,21,38,55,72,89-Hexaoxa-8,17,25,34,42,51,59,68,76,85-decathia-3,5,20,22,37,39,54,56,71,73,88,90-dodecasiladononaconta-1,91-diene, 3,3,5,5,20,20,22,22,37,37,39,39,54,54,56,56,71,71,73,73,88,88,90,90-tetracosamethyl- (9CI) (CA INDEX NAME)

FS 3D CONCORD
MF C88 H198 O6 S10 Si12
SR CA
LC STN Files: CA, CAPLUS

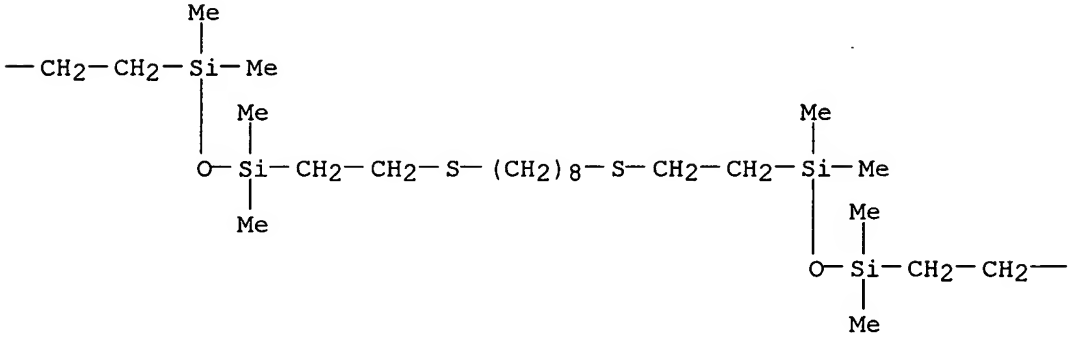
PAGE 1-A



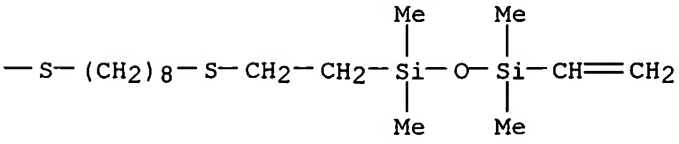
PAGE 1-B



PAGE 1-C



PAGE 1-D



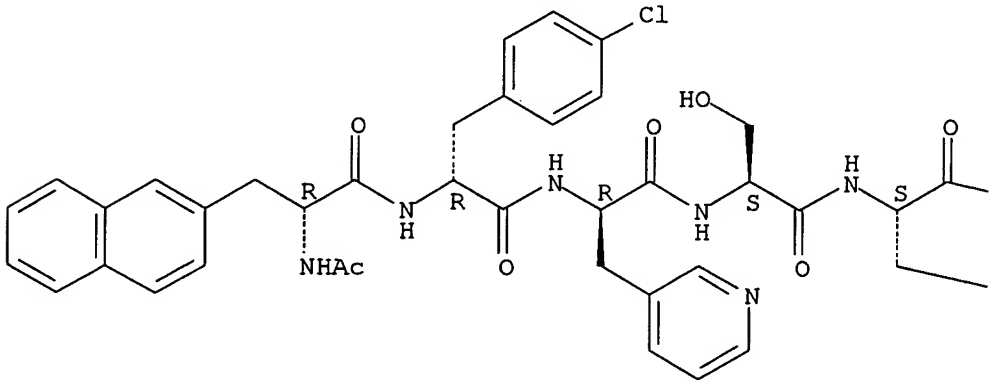
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

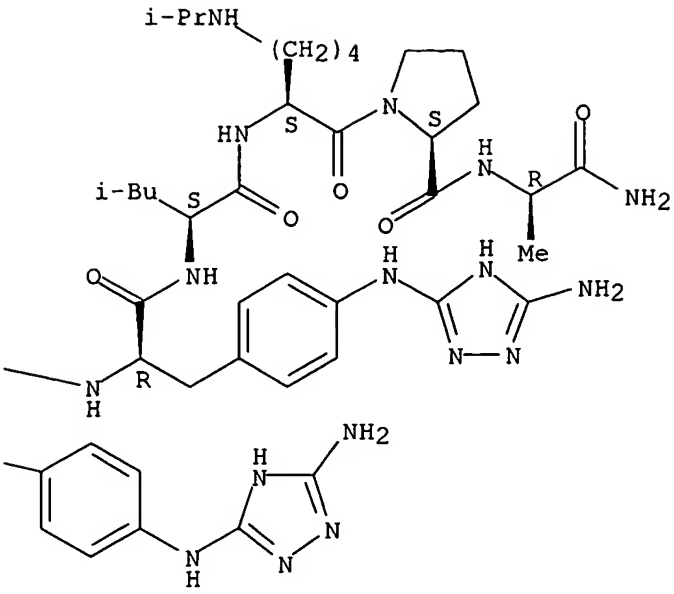
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L2 ANSWER 6 OF 12 REGISTRY COPYRIGHT 2006 ACS on STN
RN 134457-28-6 REGISTRY
ED Entered STN: 28 Jun 1991
CN D-Alaninamide, N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-D-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-4-[(5-amino-1H-1,2,4-triazol-3-yl)amino]-L-phenylalanyl-4-[(5-amino-1H-1,2,4-triazol-3-yl)amino]-D-phenylalanyl-L-leucyl-N6-(1-methylethyl)-L-lysyl-L-prolyl- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Azaline B
CN Prazarelix
CN RWJ 47428-099
FS PROTEIN SEQUENCE; STEREOSEARCH
DR 188405-77-8
MF C80 H102 Cl N23 O12
CI COM
SR CA
LC STN Files: BEILSTEIN*, BIOSIS, CA, CAPLUS, RTECS*, TOXCENTER, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)

RELATED SEQUENCES AVAILABLE WITH SEQLINK

Absolute stereochemistry.





PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

35 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
35 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L2 ANSWER 7 OF 12 REGISTRY COPYRIGHT 2006 ACS on STN
RN 129311-55-3 REGISTRY
ED Entered STN: 14 Sep 1990
CN D-Alaninamide, N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-D-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-L-tyrosyl-N6-[bis(ethylamino)methylene]-D-lysyl-L-leucyl-N6-[bis(ethylamino)methylene]-L-lysyl-L-prolyl-, diacetate (salt) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Antagon
CN Ganirelix acetate
FS PROTEIN SEQUENCE; STEREOSEARCH
MF C80 H113 Cl N18 O13 . 2 C2 H4 O2
SR US Adopted Names Council (USAN)
LC STN Files: ADISINSIGHT, BIOSIS, BIOTECHNO, CA, CAPLUS, CIN, EMBASE, IMSPATENTS, IMSRESEARCH, IPA, MRCK*, PROUSDDR, PS, SYNTHLINE, TOXCENTER, USAN
(*File contains numerically searchable property data)

RELATED SEQUENCES AVAILABLE WITH SEQLINK

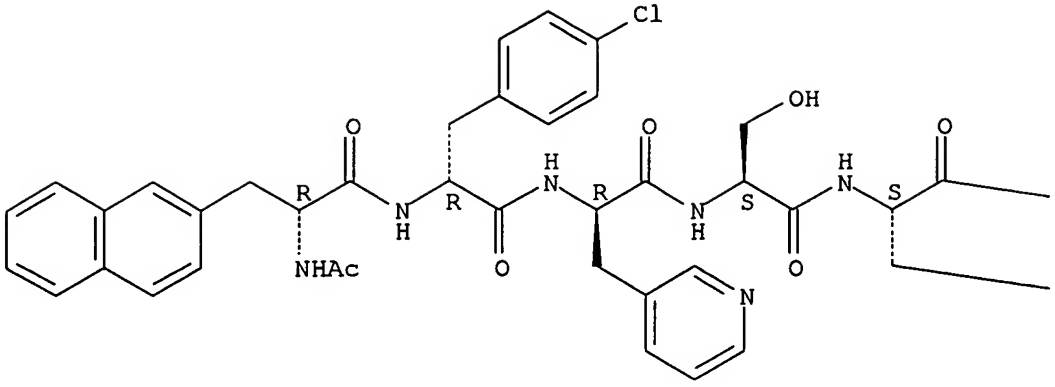
CM 1

CRN 124904-93-4
CMF C80 H113 Cl N18 O13

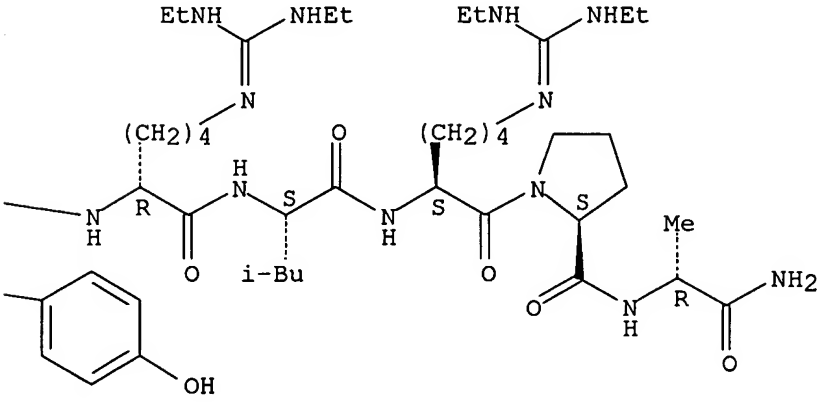
RELATED SEQUENCES AVAILABLE WITH SEQLINK

Absolute stereochemistry.

PAGE 1-A

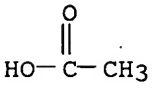


PAGE 1-B



CM 2

CRN 64-19-7
CMF C2 H4 O2



16 REFERENCES IN FILE CA (1907 TO DATE)
16 REFERENCES IN FILE CAPLUS (1907 TO DATE)

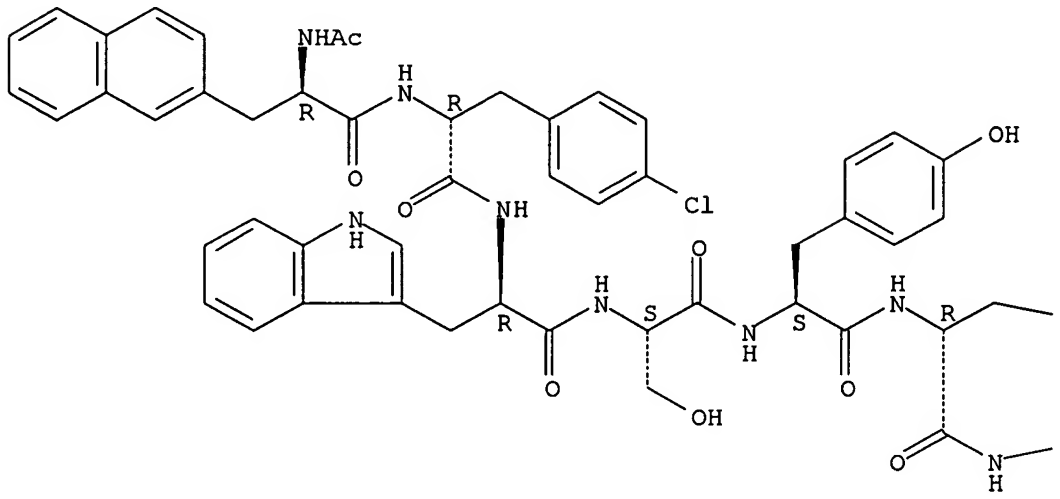
L2 ANSWER 8 OF 12 REGISTRY COPYRIGHT 2006 ACS on STN
RN 127932-90-5 REGISTRY
ED Entered STN: 29 Jun 1990
CN L-Proline, N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-D-phenylalanyl-D-tryptophyl-L-seryl-L-tyrosyl-O-(6-deoxy-α-L-mannopyranosyl)-D-seryl-L-leucyl-L-arginyl-, 2-(aminocarbonyl)hydrazide (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN L-Proline, 1-[N2-[N-[N-[N-[N-[N-[N-[N-acetyl-3-(2-naphthalenyl)-D-alanyl]-4-chloro-D-phenylalanyl]-D-tryptophyl]-L-seryl]-L-tyrosyl]-O-(6-deoxy-α-L-mannopyranosyl)-D-seryl]-L-leucyl]-L-arginyl]-, 2-(aminocarbonyl)hydrazide

OTHER NAMES:
CN HOE 013
CN Ramorelix
FS PROTEIN SEQUENCE; STEREOSEARCH
DR 136639-71-9
MF C74 H95 Cl N16 O18
SR CA
LC STN Files: ADISINSIGHT, ADISNEWS, BIOSIS, CA, CAPLUS, IMSDRUGNEWS, IMSRESEARCH, MEDLINE, PHAR, PROMT, PROUSDDR, TOXCENTER, USAN, USPAT2, USPATFULL

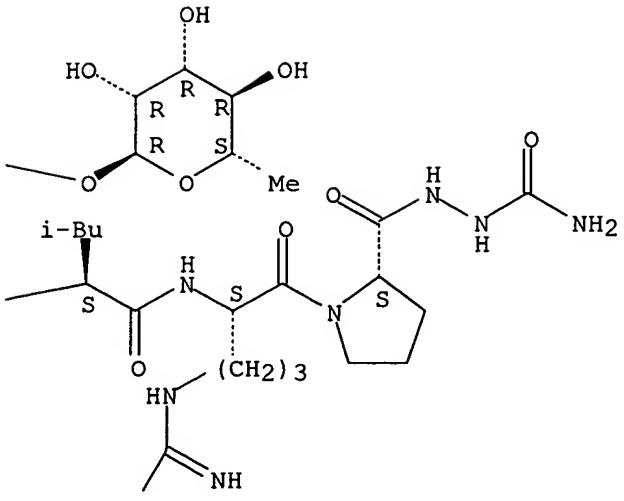
RELATED SEQUENCES AVAILABLE WITH SEQLINK

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



H_2N

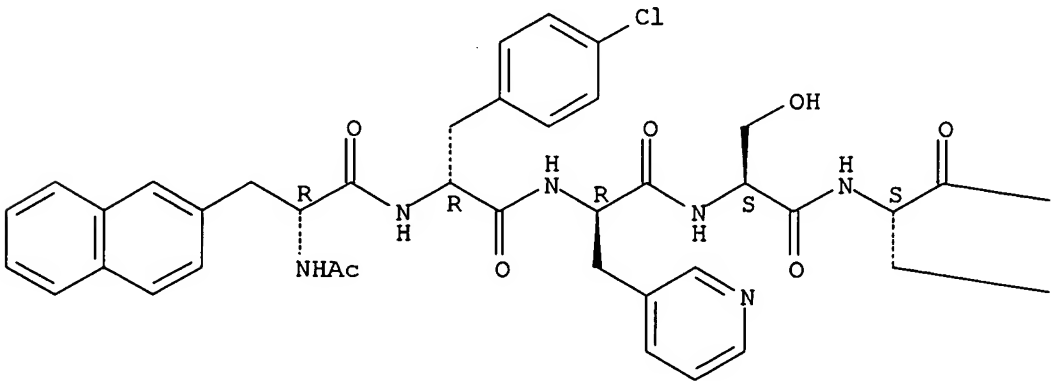
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

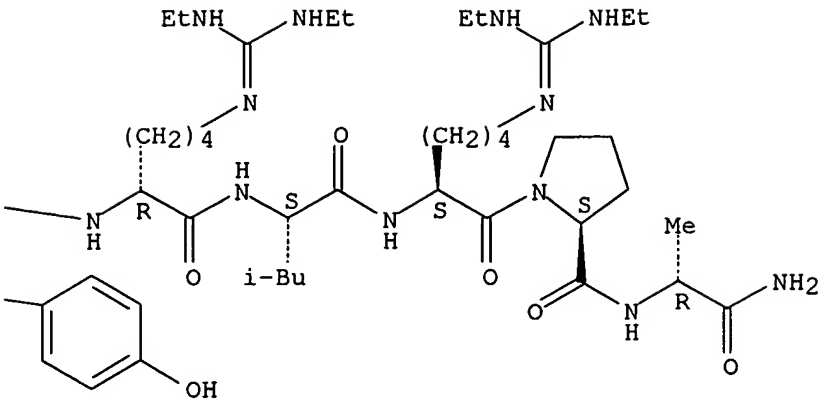
33 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
33 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L2 ANSWER 9 OF 12 REGISTRY COPYRIGHT 2006 ACS on STN
RN 124904-93-4 REGISTRY
ED Entered STN: 19 Jan 1990
CN D-Alaninamide, N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-D-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-L-tyrosyl-N6-[bis(ethylamino)methylene]-D-lysyl-L-leucyl-N6-[bis(ethylamino)methylene]-L-lysyl-L-prolyl- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN D 24598
CN Ganirelix
CN Orgalutran
CN RS 26306
FS PROTEIN SEQUENCE; STEREOSEARCH
DR 123246-29-7, 181372-97-4
MF C80 H113 Cl N18 O13
CI COM
SR CA
LC STN Files: ADISINSIGHT, ADISNEWS, BIOSIS, BIOTECHNO, CA, CAPLUS, DDFU, DRUGU, EMBASE, IMSDRUGNEWS, IMSPATENTS, IMSRESEARCH, IPA, MEDLINE, MRCK*, PATDPASPC, PHAR, PROMT, PROUSDDR, PS, RTECS*, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: WHO

RELATED SEQUENCES AVAILABLE WITH SEQLINK

Absolute stereochemistry.





PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

136 REFERENCES IN FILE CA (1907 TO DATE)
4 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
137 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L2 ANSWER 10 OF 12 REGISTRY COPYRIGHT 2006 ACS on STN
RN 108021-99-4 REGISTRY
ED Entered STN: 09 May 1987
CN Cytochrome c (cattle protein moiety reduced), 5-[6-(2,5-dihydro-3-methyl-2,5-dioxo-1H-pyrrol-1-yl)-L-norleucine]-7-[6-(2,5-dihydro-3-methyl-2,5-dioxo-1H-pyrrol-1-yl)-L-norleucine]-8-[6-(2,5-dihydro-3-methyl-2,5-dioxo-1H-pyrrol-1-yl)-L-norleucine]-13-[6-(2,5-dihydro-3-methyl-2,5-dioxo-1H-pyrrol-1-yl)-L-norleucine]-14-[S-(2-amino-2-oxoethyl)-L-cysteine]-17-[S-(2-amino-2-oxoethyl)-L-cysteine]-22-[6-(2,5-dihydro-3-methyl-2,5-dioxo-1H-pyrrol-1-yl)-L-norleucine]-25-[6-(2,5-dihydro-3-methyl-2,5-dioxo-1H-pyrrol-1-yl)-L-norleucine]-27-[6-(2,5-dihydro-3-methyl-2,5-dioxo-1H-pyrrol-1-yl)-L-norleucine]-39-[6-(2,5-dihydro-3-methyl-2,5-dioxo-1H-pyrrol-1-yl)-L-norleucine]-53-[6-(2,5-dihydro-3-methyl-2,5-dioxo-1H-pyrrol-1-yl)-L-norleucine]-55-[6-(2,5-dihydro-3-methyl-2,5-dioxo-1H-pyrrol-1-yl)-L-norleucine]-72-[6-(2,5-dihydro-3-methyl-2,5-dioxo-1H-pyrrol-1-yl)-L-norleucine]-73-[6-(2,5-dihydro-3-methyl-2,5-dioxo-1H-pyrrol-1-yl)-L-norleucine]-79-[6-(2,5-dihydro-3-methyl-2,5-dioxo-1H-pyrrol-1-yl)-L-norleucine]-86-[6-(2,5-dihydro-3-methyl-2,5-dioxo-1H-pyrrol-1-yl)-L-norleucine]-87-[6-(2,5-dihydro-3-methyl-2,5-dioxo-1H-pyrrol-1-yl)-L-norleucine]-88-[6-(2,5-dihydro-3-methyl-2,5-dioxo-1H-pyrrol-1-yl)-L-norleucine]-99-[6-(2,5-dihydro-3-methyl-2,5-dioxo-1H-pyrrol-1-yl)-L-norleucine]-100-[6-(2,5-dihydro-3-methyl-2,5-dioxo-1H-pyrrol-1-yl)-L-norleucine]- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Cytochrome c (ox protein moiety reduced), 5-[6-(2,5-dihydro-3-methyl-2,5-dioxo-1H-pyrrol-1-yl)-L-norleucine]-7-[6-(2,5-dihydro-3-methyl-2,5-dioxo-1H-pyrrol-1-yl)-L-norleucine]-8-[6-(2,5-dihydro-3-methyl-2,5-dioxo-1H-pyrrol-1-yl)-L-norleucine]-13-[6-(2,5-dihydro-3-methyl-2,5-dioxo-1H-pyrrol-1-yl)-L-norleucine]-14-[S-(2-amino-2-oxoethyl)-L-cysteine]-17-[S-(2-amino-2-oxoethyl)-L-cysteine]-22-[6-(2,5-dihydro-3-methyl-2,5-dioxo-1H-pyrrol-1-yl)-L-norleucine]-25-[6-(2,5-dihydro-3-methyl-2,5-dioxo-1H-pyrrol-1-yl)-L-norleucine]-27-[6-(2,5-dihydro-3-methyl-2,5-dioxo-1H-pyrrol-1-yl)-L-norleucine]-39-[6-(2,5-dihydro-3-methyl-2,5-dioxo-1H-pyrrol-1-yl)-L-norleucine]-53-[6-(2,5-dihydro-3-methyl-2,5-dioxo-1H-pyrrol-1-yl)-L-norleucine]-55-[6-(2,5-dihydro-3-methyl-2,5-dioxo-1H-pyrrol-1-yl)-L-norleucine]-72-[6-(2,5-dihydro-3-methyl-2,5-dioxo-1H-pyrrol-1-yl)-L-norleucine]-73-[6-(2,5-dihydro-3-methyl-2,5-dioxo-1H-pyrrol-1-yl)-L-norleucine]-79-[6-(2,5-dihydro-3-methyl-2,5-dioxo-1H-pyrrol-1-yl)-L-norleucine]-86-[6-(2,5-dihydro-3-methyl-2,5-dioxo-1H-pyrrol-1-yl)-L-

```
     norleucine]-87-[6-(2,5-dihydro-3-methyl-2,5-dioxo-1H-pyrrol-1-yl)-L-
     norleucine]-88-[6-(2,5-dihydro-3-methyl-2,5-dioxo-1H-pyrrol-1-yl)-L-
     norleucine]-99-[6-(2,5-dihydro-3-methyl-2,5-dioxo-1H-pyrrol-1-yl)-L-
     norleucine]-100-[6-(2,5-dihydro-3-methyl-2,5-dioxo-1H-pyrrol-1-yl)-L-
     norleucine]-
FS   PROTEIN SEQUENCE
MF   Unspecified
CI   MAN
SR   CA
LC   STN Files:   CA, CAPLUS, CASREACT

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***
               1 REFERENCES IN FILE CA (1907 TO DATE)
               1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L2   ANSWER 11 OF 12  REGISTRY  COPYRIGHT 2006 ACS on STN
RN   91791-47-8  REGISTRY
ED   Entered STN:  16 Nov 1984
CN   Copper alloy, base, Cu 12-98,Ni 1.6-88 (9CI)  (CA INDEX NAME)
OTHER NAMES:
CN   Copper 11.12-98.26, nickel 1.74-88.88 (atomic)
MF   Cu . Ni
CI   AYS
LC   STN Files:   CA, CAPLUS

Component   Component      Component
             Percent    Registry Number
=========+=============+===============
    Cu     12   -  98       7440-50-8
    Ni      1.6 -  88       7440-02-0

               1 REFERENCES IN FILE CA (1907 TO DATE)
               1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L2   ANSWER 12 OF 12  REGISTRY  COPYRIGHT 2006 ACS on STN
RN   83746-45-6  REGISTRY
ED   Entered STN:  16 Nov 1984
CN   Nickel alloy, base, Ni 94,Al 5.6-5.9 (9CI)  (CA INDEX NAME)
OTHER NAMES:
CN   Aluminum 11.5-12, nickel 88-88.5 (atomic)
MF   Al . Ni
CI   AYS
LC   STN Files:   CA, CAPLUS

Component   Component      Component
             Percent    Registry Number
=========+=============+===============
    Ni         94           7440-02-0
    Al      5.6 -   5.9     7429-90-5

               1 REFERENCES IN FILE CA (1907 TO DATE)
               1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

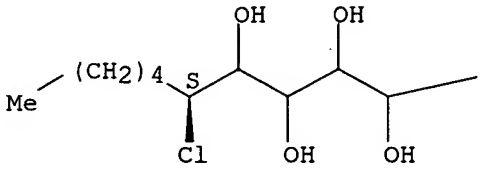

=> s 88 88
         40942 88
         40942 88
L3           6 88 88
                (88(W)88)

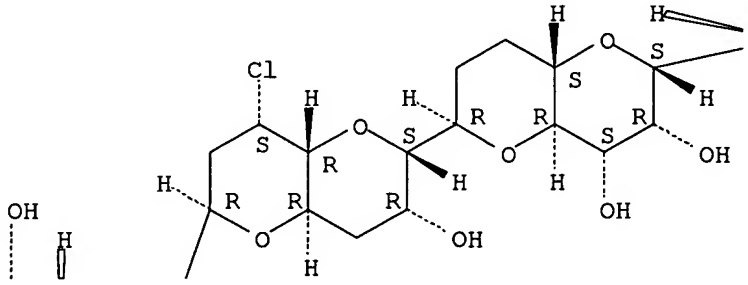
=> d 1-6
```

L3 ANSWER 1 OF 6 REGISTRY COPYRIGHT 2006 ACS on STN
RN 221381-62-0 REGISTRY
ED Entered STN: 21 Apr 1999
CN Prymnesin 2, 1-dechloro-1,2,3,3,4,4,7,7,8,8,9,10,11,12,16,17,18,19,87
,87,88,88,89,89,90,90-hexacosahydro- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 1-Dechloroperhydroprymnesin 2
FS STEREOSEARCH
MF C96 H163 Cl2 N O35
SR CA
LC STN Files: CA, CAPLUS, CASREACT, TOXCENTER

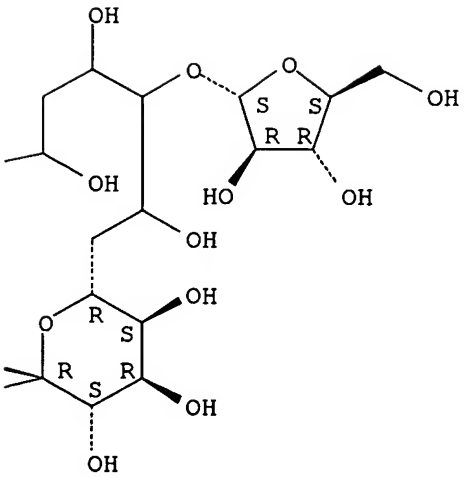
Absolute stereochemistry.
Currently available stereo shown.

PAGE 1-B

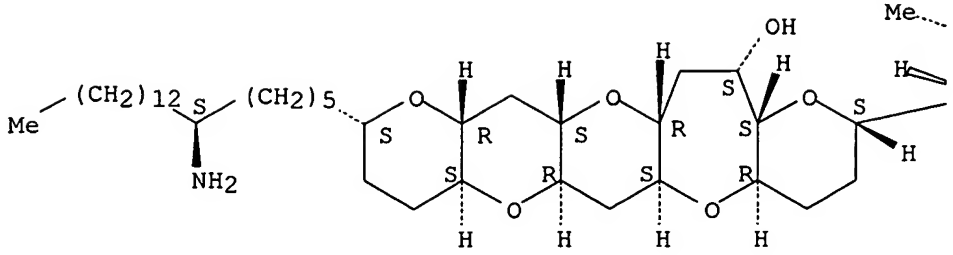




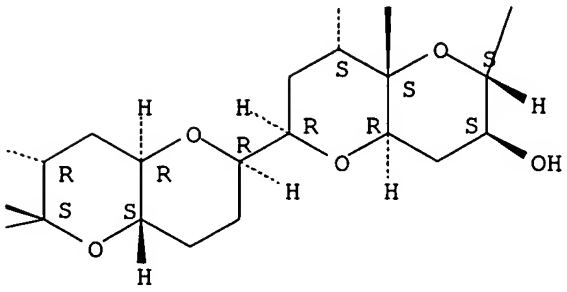
PAGE 1-C



PAGE 2-A



PAGE 2-B



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L3 ANSWER 2 OF 6 REGISTRY COPYRIGHT 2006 ACS on STN
RN 168849-75-0 REGISTRY
ED Entered STN: 13 Oct 1995
CN 79,101-(Methanoxy[1,4]benzenomethano[1,4]benzenoxymethano)-9,12:14,17:47,50:52,55-tetraetheno-27,31:71,75-dimethano-41,61-(methanoxy[1,4]benzenomethano[1,4]benzenoxymethano)-2,66:3,65:23,37:24,36-tetrametheno-1H,7H,13H,19H,25H,33H,35H,45H,51H,57H,67H,69H-bis[1,3]benzodioxocino[9,8-d:9',8'-d']bis[1,3]benzodioxocino[9',10':24,25;10'',9'':39,40][1,3,7,17,21,23,27,37], octaoxacyclotetracontino[4,5-j:20,19-j']bis[1,3]benzodioxocin, 1,25,33,35,67,69,77,103-octapentyl-13,13,51,51,88,88,116,116-octakis(trifluoromethyl)-, stereoisomer (9CI) (CA INDEX NAME)
MF C172 H168 F24 O24
SR CA
LC STN Files: CA, CAPLUS, CASREACT

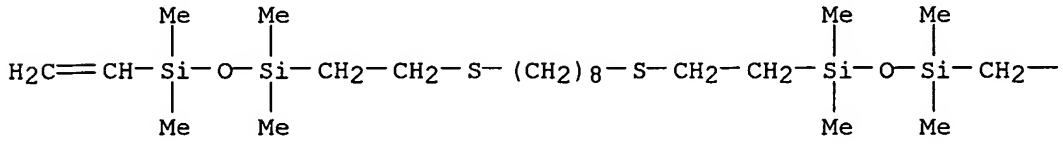
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L3 ANSWER 3 OF 6 REGISTRY COPYRIGHT 2006 ACS on STN
RN 134798-68-8 REGISTRY
ED Entered STN: 12 Jul 1991
CN 4,21,38,55,72,89-Hexaoxa-8,17,25,34,42,51,59,68,76,85-decathia-

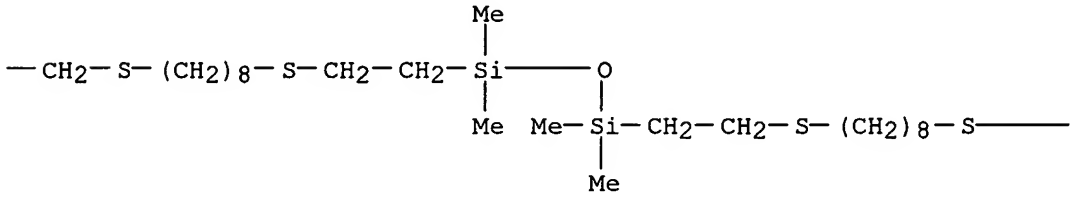
3,5,20,22,37,39,54,56,71,73,88,90-dodecasiladononaconta-1,91-diene, 3,3,5,5,20,20,22,22,37,37,39,39,54,54,56,56,71,71,73,73,88,88,90,90-tetracosamethyl- (9CI) (CA INDEX NAME)

FS 3D CONCORD
MF C88 H198 O6 S10 Si12
SR CA
LC STN Files: CA, CAPLUS

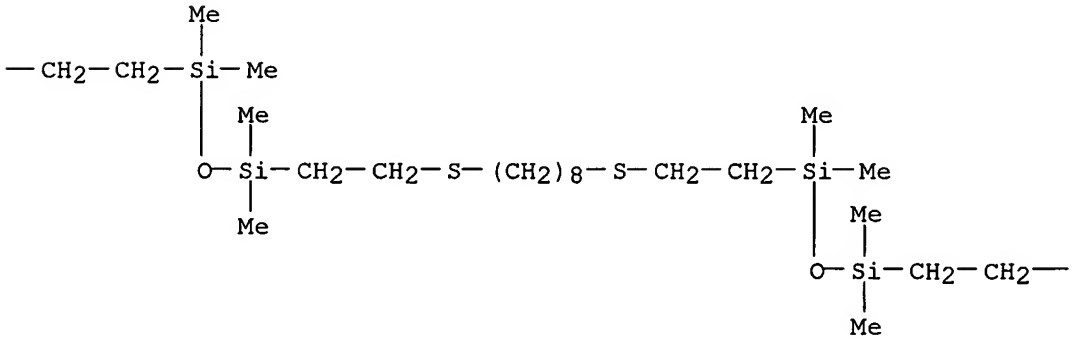
PAGE 1-A

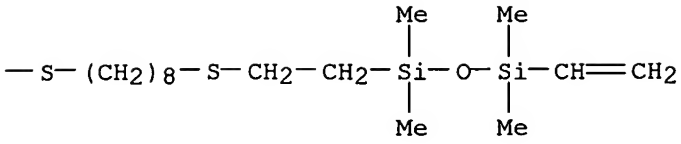


PAGE 1-B



PAGE 1-C





PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L3 ANSWER 4 OF 6 REGISTRY COPYRIGHT 2006 ACS on STN
RN 108021-99-4 REGISTRY
ED Entered STN: 09 May 1987
CN Cytochrome c (cattle protein moiety reduced), 5-[6-(2,5-dihydro-3-methyl-2,5-dioxo-1H-pyrrol-1-yl)-L-norleucine]-7-[6-(2,5-dihydro-3-methyl-2,5-dioxo-1H-pyrrol-1-yl)-L-norleucine]-8-[6-(2,5-dihydro-3-methyl-2,5-dioxo-1H-pyrrol-1-yl)-L-norleucine]-13-[6-(2,5-dihydro-3-methyl-2,5-dioxo-1H-pyrrol-1-yl)-L-norleucine]-14-[S-(2-amino-2-oxoethyl)-L-cysteine]-17-[S-(2-amino-2-oxoethyl)-L-cysteine]-22-[6-(2,5-dihydro-3-methyl-2,5-dioxo-1H-pyrrol-1-yl)-L-norleucine]-25-[6-(2,5-dihydro-3-methyl-2,5-dioxo-1H-pyrrol-1-yl)-L-norleucine]-27-[6-(2,5-dihydro-3-methyl-2,5-dioxo-1H-pyrrol-1-yl)-L-norleucine]-39-[6-(2,5-dihydro-3-methyl-2,5-dioxo-1H-pyrrol-1-yl)-L-norleucine]-53-[6-(2,5-dihydro-3-methyl-2,5-dioxo-1H-pyrrol-1-yl)-L-norleucine]-55-[6-(2,5-dihydro-3-methyl-2,5-dioxo-1H-pyrrol-1-yl)-L-norleucine]-72-[6-(2,5-dihydro-3-methyl-2,5-dioxo-1H-pyrrol-1-yl)-L-norleucine]-73-[6-(2,5-dihydro-3-methyl-2,5-dioxo-1H-pyrrol-1-yl)-L-norleucine]-79-[6-(2,5-dihydro-3-methyl-2,5-dioxo-1H-pyrrol-1-yl)-L-norleucine]-86-[6-(2,5-dihydro-3-methyl-2,5-dioxo-1H-pyrrol-1-yl)-L-norleucine]-87-[6-(2,5-dihydro-3-methyl-2,5-dioxo-1H-pyrrol-1-yl)-L-norleucine]-88-[6-(2,5-dihydro-3-methyl-2,5-dioxo-1H-pyrrol-1-yl)-L-norleucine]-99-[6-(2,5-dihydro-3-methyl-2,5-dioxo-1H-pyrrol-1-yl)-L-norleucine]-100-[6-(2,5-dihydro-3-methyl-2,5-dioxo-1H-pyrrol-1-yl)-L-norleucine]- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Cytochrome c (ox protein moiety reduced), 5-[6-(2,5-dihydro-3-methyl-2,5-dioxo-1H-pyrrol-1-yl)-L-norleucine]-7-[6-(2,5-dihydro-3-methyl-2,5-dioxo-1H-pyrrol-1-yl)-L-norleucine]-8-[6-(2,5-dihydro-3-methyl-2,5-dioxo-1H-pyrrol-1-yl)-L-norleucine]-13-[6-(2,5-dihydro-3-methyl-2,5-dioxo-1H-pyrrol-1-yl)-L-norleucine]-14-[S-(2-amino-2-oxoethyl)-L-cysteine]-17-[S-(2-amino-2-oxoethyl)-L-cysteine]-22-[6-(2,5-dihydro-3-methyl-2,5-dioxo-1H-pyrrol-1-yl)-L-norleucine]-25-[6-(2,5-dihydro-3-methyl-2,5-dioxo-1H-pyrrol-1-yl)-L-norleucine]-27-[6-(2,5-dihydro-3-methyl-2,5-dioxo-1H-pyrrol-1-yl)-L-norleucine]-39-[6-(2,5-dihydro-3-methyl-2,5-dioxo-1H-pyrrol-1-yl)-L-norleucine]-53-[6-(2,5-dihydro-3-methyl-2,5-dioxo-1H-pyrrol-1-yl)-L-norleucine]-55-[6-(2,5-dihydro-3-methyl-2,5-dioxo-1H-pyrrol-1-yl)-L-norleucine]-72-[6-(2,5-dihydro-3-methyl-2,5-dioxo-1H-pyrrol-1-yl)-L-norleucine]-73-[6-(2,5-dihydro-3-methyl-2,5-dioxo-1H-pyrrol-1-yl)-L-norleucine]-79-[6-(2,5-dihydro-3-methyl-2,5-dioxo-1H-pyrrol-1-yl)-L-norleucine]-86-[6-(2,5-dihydro-3-methyl-2,5-dioxo-1H-pyrrol-1-yl)-L-norleucine]-87-[6-(2,5-dihydro-3-methyl-2,5-dioxo-1H-pyrrol-1-yl)-L-

```
     norleucine]-88-[6-(2,5-dihydro-3-methyl-2,5-dioxo-1H-pyrrol-1-yl)-L-
     norleucine]-99-[6-(2,5-dihydro-3-methyl-2,5-dioxo-1H-pyrrol-1-yl)-L-
     norleucine]-100-[6-(2,5-dihydro-3-methyl-2,5-dioxo-1H-pyrrol-1-yl)-L-
     norleucine]-
FS   PROTEIN SEQUENCE
MF   Unspecified
CI   MAN
SR   CA
LC   STN Files:   CA, CAPLUS, CASREACT

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***
               1 REFERENCES IN FILE CA (1907 TO DATE)
               1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L3   ANSWER 5 OF 6  REGISTRY  COPYRIGHT 2006 ACS on STN
RN   91791-47-8  REGISTRY
ED   Entered STN:  16 Nov 1984
CN   Copper alloy, base, Cu 12-98,Ni 1.6-88 (9CI)  (CA INDEX NAME)
OTHER NAMES:
CN   Copper 11.12-98.26, nickel 1.74-88.88 (atomic)
MF   Cu . Ni
CI   AYS
LC   STN Files:   CA, CAPLUS

Component   Component      Component
             Percent    Registry Number
=========+=============+===============
    Cu     12   -  98       7440-50-8
    Ni      1.6 -  88       7440-02-0

               1 REFERENCES IN FILE CA (1907 TO DATE)
               1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L3   ANSWER 6 OF 6  REGISTRY  COPYRIGHT 2006 ACS on STN
RN   83746-45-6  REGISTRY
ED   Entered STN:  16 Nov 1984
CN   Nickel alloy, base, Ni 94,Al 5.6-5.9 (9CI)  (CA INDEX NAME)
OTHER NAMES:
CN   Aluminum 11.5-12, nickel 88-88.5 (atomic)
MF   Al . Ni
CI   AYS
LC   STN Files:   CA, CAPLUS

Component   Component      Component
             Percent    Registry Number
=========+=============+===============
    Ni         94           7440-02-0
    Al      5.6 -   5.9     7429-90-5

               1 REFERENCES IN FILE CA (1907 TO DATE)
               1 REFERENCES IN FILE CAPLUS (1907 TO DATE)


=> d his

     (FILE 'HOME' ENTERED AT 15:35:15 ON 21 AUG 2006)

     FILE 'REGISTRY' ENTERED AT 15:35:28 ON 21 AUG 2006
L1            4 S CETRORELIX
L2           12 S GANIRELIX OR ANATARELIX ANTIDE OR AZALINE B OR RAMORELIX OR A
L3            6 S 88 88
```

```
=> file caplus medline biosis embase uspatful
COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                       114.96     115.17

FILE 'CAPLUS' ENTERED AT 15:37:37 ON 21 AUG 2006
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2006 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'MEDLINE' ENTERED AT 15:37:37 ON 21 AUG 2006

FILE 'BIOSIS' ENTERED AT 15:37:37 ON 21 AUG 2006
Copyright (c) 2006 The Thomson Corporation

FILE 'EMBASE' ENTERED AT 15:37:37 ON 21 AUG 2006
Copyright (c) 2006 Elsevier B.V. All rights reserved.

FILE 'USPATFULL' ENTERED AT 15:37:37 ON 21 AUG 2006
CA INDEXING COPYRIGHT (C) 2006 AMERICAN CHEMICAL SOCIETY (ACS)

=> s cetrorelix or cetrotid or cetrotide or 145672-81-7/rn or 120287-85-6/rn
'RN' IS NOT A VALID FIELD CODE
'RN' IS NOT A VALID FIELD CODE
'RN' IS NOT A VALID FIELD CODE
L4          2206 CETRORELIX OR CETROTID OR CETROTIDE OR 145672-81-7/RN OR 120287-
                 85-6/RN

=> s l4 and (infertility or fertility or pregnancy or sterility or reductive? )
L5           857 L4 AND (INFERTILITY OR FERTILITY OR PREGNANCY OR STERILITY OR
                 REDUCTIVE? )

=> dup rem l5
PROCESSING COMPLETED FOR L5
L6           604 DUP REM L5 (253 DUPLICATES REMOVED)

=> s hmg or gonadotripin or fsh or clomiphene or clomiphen or clomifene of clomifen
   4 FILES SEARCHED...
L7        166334 HMG OR GONADOTRIPIN OR FSH OR CLOMIPHENE OR CLOMIPHEN OR CLOMIFE
                 NE OF CLOMIFEN

=> s l6 and l7
L8           229 L6 AND L7

=> dup rem l8
PROCESSING COMPLETED FOR L8
L9           229 DUP REM L8 (0 DUPLICATES REMOVED)

=> l9 and (hmg or fsh or folicular stimulating hormone or gonadotropin)
L9 IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> s l9 and (hmg or fsh or folicular stimulating hormone or gonadotropin)
L10          228 L9 AND (HMG OR FSH OR FOLICULAR STIMULATING HORMONE OR GONADOTR
                 OPIN)

=> file reg
COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                        59.34     174.51
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FILE 'REGISTRY' ENTERED AT 15:43:56 ON 21 AUG 2006

Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES: 20 AUG 2006 HIGHEST RN 902860-89-3
DICTIONARY FILE UPDATES: 20 AUG 2006 HIGHEST RN 902860-89-3

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH June 30, 2006

Please note that search-term pricing does apply when
conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and
predicted properties as well as tags indicating availability of
experimental property data in the original document. For information
on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

=> s clomiphene
L11 9 CLOMIPHENE

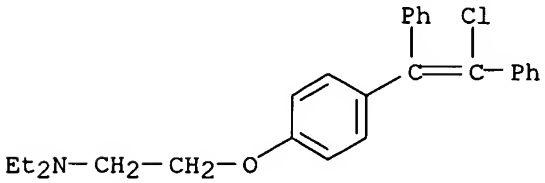
=> d l11 9-9

L11 ANSWER 9 OF 9 REGISTRY COPYRIGHT 2006 ACS on STN
RN 50-41-9 REGISTRY
ED Entered STN: 16 Nov 1984
CN Ethanamine, 2-[4-(2-chloro-1,2-diphenylethenyl)phenoxy]-N,N-diethyl-,
2-hydroxy-1,2,3-propanetricarboxylate (1:1) (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Triethylamine, 2-[p-(2-chloro-1,2-diphenylvinyl)phenoxy]-, citrate (6CI,
7CI)
CN Triethylamine, 2-[p-(2-chloro-1,2-diphenylvinyl)phenoxy]-, citrate (1:1)
(8CI)
OTHER NAMES:
CN 1-[p-(β-Diethylaminoethoxy)phenyl]-1,2-diphenyl-2-chloroethylene
citrate
CN 2-[p-(2-Chloro-1,2-diphenylvinyl)phenoxy]triethylamine dihydrogen citrate
CN Chloramiphene
CN Clomid
CN Clomifene citrate
CN Clomifeno
CN Clomiphene citrate
CN Clomiphene dihydrogen citrate
CN Clomivid
CN Clomphid
CN Clostilbegit
CN Clostilbegyt
CN Dyneric
CN Fertivet
CN Fertyl
CN Genozym
CN Ikaclomin
CN Ikaclomine
CN Mer 41
CN MRL 41
CN NSC 35770

CN Omifin
CN Pergotime
CN Racemic clomiphene citrate
CN Serophene
MF C26 H28 Cl N O . C6 H8 O7
CI COM
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOSIS, BIOTECHNO, CA, CAOLD, CAPLUS, CBNB, CHEMCATS, CHEMLIST, CIN, CSCHEM, CSNB, EMBASE, HSDB*, IFICDB, IFIPAT, IFIUDB, IMSCOSEARCH, IPA, MRCK*, MSDS-OHS, PROMT, PS, RTECS*, TOXCENTER, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: EINECS**
(**Enter CHEMLIST File for up-to-date regulatory information)

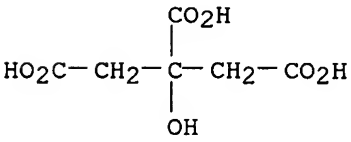
CM 1

CRN 911-45-5
CMF C26 H28 Cl N O



CM 2

CRN 77-92-9
CMF C6 H8 O7



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

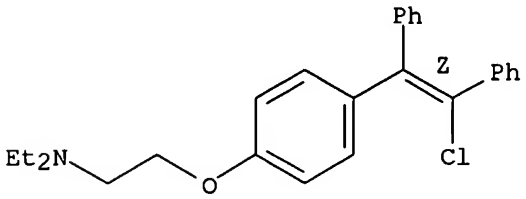
855 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
856 REFERENCES IN FILE CAPLUS (1907 TO DATE)
25 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

=> d 5-9

L11 ANSWER 5 OF 9 REGISTRY COPYRIGHT 2006 ACS on STN
RN 15690-55-8 REGISTRY
ED Entered STN: 16 Nov 1984
CN Ethanamine, 2-[4-[(1Z)-2-chloro-1,2-diphenylethenyl]phenoxy]-N,N-diethyl- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Ethanamine, 2-[4-(2-chloro-1,2-diphenylethenyl)phenoxy]-N,N-diethyl-, (Z)-
CN Triethylamine, 2-[p-(2-chloro-1,2-diphenylvinyl)phenoxy]-, (Z)- (8CI)
OTHER NAMES:
CN (Z)-Clomiphene

CN cis-Clomifene
CN cis-Clomiphene
CN RMI 16312
CN Zuclomifene
CN Zuclomiphene
FS STEREOSEARCH
MF C26 H28 Cl N O
CI COM
LC STN Files: AGRICOLA, BEILSTEIN*, BIOSIS, BIOTECHNO, CA, CAPLUS, CASREACT, CHEMCATS, CHEMINFORMRX, CHEMLIST, DDFU, DRUGU, EMBASE, IFICDB, IFIPAT, IFIUDB, IPA, MRCK*, RTECS*, TOXCENTER, USAN, USPATFULL
(*File contains numerically searchable property data)
Other Sources: WHO

Double bond geometry as shown.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

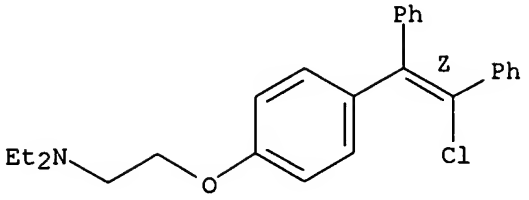
130 REFERENCES IN FILE CA (1907 TO DATE)
130 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L11 ANSWER 6 OF 9 REGISTRY COPYRIGHT 2006 ACS on STN
RN 7619-53-6 REGISTRY
ED Entered STN: 16 Nov 1984
CN Ethanamine, 2-[4-[(1Z)-2-chloro-1,2-diphenylethenyl]phenoxy]-N,N-diethyl-, 2-hydroxy-1,2,3-propanetricarboxylate (1:1) (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Ethanamine, 2-[4-(2-chloro-1,2-diphenylethenyl)phenoxy]-N,N-diethyl-, (Z)-, 2-hydroxy-1,2,3-propanetricarboxylate (1:1)
CN Triethylamine, 2-[p-(2-chloro-1,2-diphenylvinyl)phenoxy]-, citrate (1:1), (Z)- (8CI)
OTHER NAMES:
CN (Z)-Clomiphene citrate
CN cis-Clomiphene citrate
CN Clomiphene A citrate
CN NSC 151466
CN Zuclomid
CN Zuclomiphene citrate
FS STEREOSEARCH
DR 207563-42-6
MF C26 H28 Cl N O . C6 H8 O7
LC STN Files: BEILSTEIN*, BIOSIS, BIOTECHNO, CA, CAPLUS, CASREACT, CHEMLIST, EMBASE, IFICDB, IFIPAT, IFIUDB, IPA, RTECS*, TOXCENTER, USPATFULL
(*File contains numerically searchable property data)

CM 1

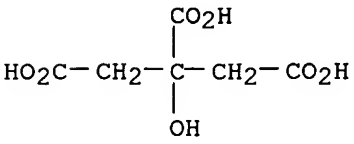
CRN 15690-55-8
CMF C26 H28 Cl N O

Double bond geometry as shown.



CM 2

CRN 77-92-9
CMF C6 H8 O7



56 REFERENCES IN FILE CA (1907 TO DATE)
56 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L11 ANSWER 7 OF 9 REGISTRY COPYRIGHT 2006 ACS on STN
RN 7599-79-3 REGISTRY
ED Entered STN: 16 Nov 1984
CN Ethanamine, 2-[4-[(1E)-2-chloro-1,2-diphenylethenyl]phenoxy]-N,N-diethyl-, 2-hydroxy-1,2,3-propanetricarboxylate (1:1) (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Ethanamine, 2-[4-(2-chloro-1,2-diphenylethenyl)phenoxy]-N,N-diethyl-, (E)-, 2-hydroxy-1,2,3-propanetricarboxylate (1:1)
CN Triethylamine, 2-[p-(2-chloro-1,2-diphenylvinyl)phenoxy]-, citrate (1:1), (E)- (8CI)
OTHER NAMES:
CN (E)-Clomiphene citrate
CN Clomiphene B citrate
CN Enclomid
CN Enclomiphene citrate
CN trans-Clomiphene citrate
FS STEREOSEARCH
DR 96189-17-2, 207562-80-9
MF C26 H28 Cl N O . C6 H8 O7
LC STN Files: BEILSTEIN*, BIOTECHNO, CA, CAPLUS, CASREACT, CHEMLIST, EMBASE, IFICDB, IFIPAT, IFIUDB, IMSRESEARCH, IPA, RTECS*, TOXCENTER, USPAT2, USPATFULL
(*File contains numerically searchable property data)

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CRN 15690-57-0
CMF C26 H28 Cl N O

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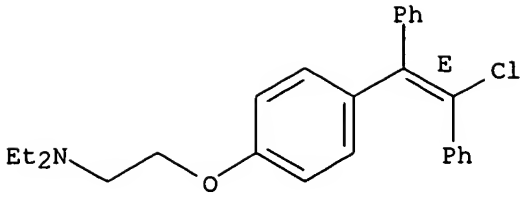

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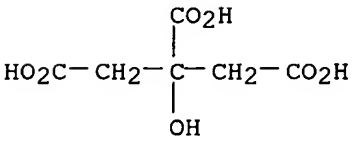

53 REFERENCES IN FILE CA (1907 TO DATE)
53 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L11 ANSWER 8 OF 9 REGISTRY COPYRIGHT 2006 ACS on STN
RN 911-45-5 REGISTRY
ED Entered STN: 16 Nov 1984
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OTHER CA INDEX NAMES:
CN Triethylamine, 2-[p-(2-chloro-1,2-diphenylvinyl)phenoxy]- (7CI, 8CI)
OTHER NAMES:
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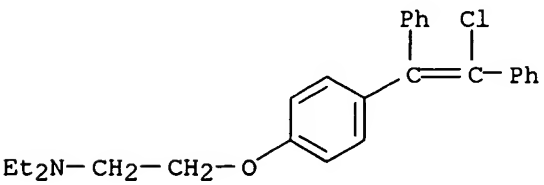
CN 2-[p-(β-Chloro-α-phenylstyryl)phenoxy]triethylamine
CN 2-[p-(2-Chloro-1,2-diphenylvinyl)phenoxy]triethylamine
CN Clomifene
CN Clomiphene
CN Clomiphene B
FS 3D CONCORD
MF C26 H28 Cl N O
CI COM
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOSIS, BIOTECHNO, CA, CABA, CAOLD, CAPLUS, CASREACT, CBNB, CHEMCATS, CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, DDFU, DRUGU, EMBASE, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, PROMT, PS, RTECS*, SPECINFO, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: EINECS**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)



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11 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
666 REFERENCES IN FILE CAPLUS (1907 TO DATE)
16 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

L11 ANSWER 9 OF 9 REGISTRY COPYRIGHT 2006 ACS on STN
RN 50-41-9 REGISTRY
ED Entered STN: 16 Nov 1984
CN Ethanamine, 2-[4-(2-chloro-1,2-diphenylethenyl)phenoxy]-N,N-diethyl-, 2-hydroxy-1,2,3-propanetricarboxylate (1:1) (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Triethylamine, 2-[p-(2-chloro-1,2-diphenylvinyl)phenoxy]-, citrate (6CI, 7CI)
CN Triethylamine, 2-[p-(2-chloro-1,2-diphenylvinyl)phenoxy]-, citrate (1:1) (8CI)
OTHER NAMES:
CN 1-[p-(β-Diethylaminoethoxy)phenyl]-1,2-diphenyl-2-chloroethylene citrate
CN 2-[p-(2-Chloro-1,2-diphenylvinyl)phenoxy]triethylamine dihydrogen citrate
CN Chloramiphene
CN Clomid
CN Clomifene citrate
CN Clomifeno
CN Clomiphene citrate
CN Clomiphene dihydrogen citrate
CN Clomivid
CN Clomphid
CN Clostilbegit
CN Clostilbegyt
CN Dyneric
CN Fertivet
CN Fertyl
CN Genozym
CN Ikaclomin
CN Ikaclomine
CN Mer 41
CN MRL 41
CN NSC 35770
CN Omifin
CN Pergotime
CN Racemic clomiphene citrate
CN Serophene
MF C26 H28 Cl N O . C6 H8 O7
CI COM
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOSIS, BIOTECHNO, CA, CAOLD, CAPLUS, CBNB, CHEMCATS, CHEMLIST, CIN, CSCHEM, CSNB, EMBASE, HSDB*, IFICDB, IFIPAT, IFIUDB, IMSCOSEARCH, IPA, MRCK*, MSDS-OHS, PROMT, PS, RTECS*, TOXCENTER, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: EINECS**
(**Enter CHEMLIST File for up-to-date regulatory information)

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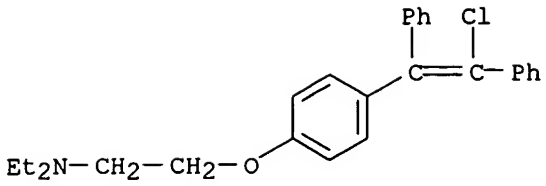
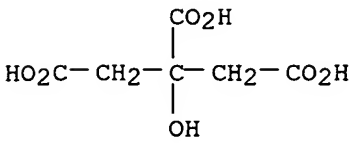
CRN 911-45-5
CMF C26 H28 Cl N O



CM 2

CRN 77-92-9
CMF C6 H8 O7



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

855 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
856 REFERENCES IN FILE CAPLUS (1907 TO DATE)
25 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

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=> file caplus medline biosis embase uspatful
COST IN U.S. DOLLARS                            SINCE FILE      TOTAL
                                                     ENTRY    SESSION
FULL ESTIMATED COST                                  17.04     191.55

FILE 'CAPLUS' ENTERED AT 15:44:57 ON 21 AUG 2006
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FILE 'USPATFULL' ENTERED AT 15:44:57 ON 21 AUG 2006
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=> d his

     (FILE 'HOME' ENTERED AT 15:35:15 ON 21 AUG 2006)

     FILE 'REGISTRY' ENTERED AT 15:35:28 ON 21 AUG 2006
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L2            12 S GANIRELIX OR ANATARELIX ANTIDE OR AZALINE B OR RAMORELIX OR A
L3             6 S 88 88

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     21 AUG 2006
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L4          2206 S CETRORELIX OR CETROTID OR CETROTIDE OR 145672-81-7/RN OR 1202
L5           857 S L4 AND (INFERTILITY OR FERTILITY OR PREGNANCY OR STERILITY OR
L6           604 DUP REM L5 (253 DUPLICATES REMOVED)
L7        166334 S HMG OR GONADOTRIPIN OR FSH OR CLOMIPHENE OR CLOMIPHEN OR CLOM
L8           229 S L6 AND L7
L9           229 DUP REM L8 (0 DUPLICATES REMOVED)
L10          228 S L9 AND (HMG OR FSH OR FOLICULAR STIMULATING HORMONE OR GONAD

     FILE 'REGISTRY' ENTERED AT 15:43:56 ON 21 AUG 2006
L11            9 S CLOMIPHENE

     FILE 'CAPLUS, MEDLINE, BIOSIS, EMBASE, USPATFULL' ENTERED AT 15:44:57 ON
     21 AUG 2006

=> s l11 or clomid or clomiphene or clomiphen or clomifene or clomifen
L12       20109 L11 OR CLOMID OR CLOMIPHENE OR CLOMIPHEN OR CLOMIFENE OR CLOMIFE
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=> s l12 and l10
L13          55 L12 AND L10

=> dup rem l13
PROCESSING COMPLETED FOR L13
L14          55 DUP REM L13 (0 DUPLICATES REMOVED)

=> focus
PROCESSING COMPLETED FOR L14
L15          55 FOCUS L14 1-

=> d ibib abs it 1-55 hitstr

L15  ANSWER 1 OF 55  USPATFULL on STN
ACCESSION NUMBER:        2004:327967  USPATFULL
TITLE:                   Inhibitors of phosphodiesterases in infertility
INVENTOR(S):             Palmer, Stephen S., Plympton, MA, UNITED STATES
                         McKenna, Sean D., Duxbury, MA, UNITED STATES
                         Arkinstall, Stephen J., Belmont, MA, UNITED STATES
                         Eshkol, Aliza, LaRippe, SWITZERLAND
                         MacNamee, Michael C., Bourn, UNITED KINGDOM

                              NUMBER         KIND    DATE
                         --------------- ------ --------
PATENT INFORMATION:      US 2004259792      A1   20041223
APPLICATION INFO.:       US 2004-817312     A1   20040401  (10)

                                NUMBER         DATE
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PRIORITY INFORMATION:    US 2003-458955P    20030401 (60)
                         US 2003-470434P    20030515 (60)
                         US 2004-540301P    20040128 (60)
                         US 2004-544003P    20040212 (60)
DOCUMENT TYPE:           Utility
FILE SEGMENT:            APPLICATION
LEGAL REPRESENTATIVE:    Attention: IP Prosecution, HOWREY SIMON ARNOLD & WHITE,
                         LLP, Box No. 34, 1299 Pennsylvania Avenue, N.W.,
                         Washington, DC, 20004-2402
NUMBER OF CLAIMS:        78
EXEMPLARY CLAIM:         1
NUMBER OF DRAWINGS:      16 Drawing Page(s)
LINE COUNT:              2555
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB     The present invention is directed to methods of increasing oocyte
       production in a mammal. More specifically, the specification describes
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methods and compositions for inducing follicular maturation using a PDE inhibitor. The inhibitor may be used alone at high doses. Alternatively, the follicular maturation is achieved by combining a low dose of FSH with the PDE inhibitor treatment.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT Gonadotropins
(combined with PDE inhibitor treatment; methods for the treatment of infertility with inhibitors of phosphodiesterases (PDE) in conjunction with gonadotropins)

IT Fertility
(disorder; methods for the treatment of infertility with inhibitors of phosphodiesterases (PDE) in conjunction with gonadotropins)

IT Ovary
(follicle, induced maturation; methods for the treatment of infertility with inhibitors of phosphodiesterases (PDE) in conjunction with gonadotropins)

IT Ovulation
(induction; methods for the treatment of infertility with inhibitors of phosphodiesterases (PDE) in conjunction with gonadotropins)

IT Drug delivery systems

IT Human
(methods for the treatment of infertility with inhibitors of phosphodiesterases (PDE) in conjunction with gonadotropins)

IT Egg
(oocyte, increased production; methods for the treatment of infertility with inhibitors of phosphodiesterases (PDE) in conjunction with gonadotropins)

IT 9002-61-3, Chorionic gonadotropin 9002-67-9, LH 9002-68-0, FSH 9002-68-0D, FSH, recombinant, urinary and human 9034-40-6, GnRH 9034-40-6D, GnRH, analog 112809-51-5, Letrozole 120511-73-1, Anastrozole 129731-10-8, Vorozole
(combined with PDE inhibitor treatment; methods for the treatment of infertility with inhibitors of phosphodiesterases (PDE) in conjunction with gonadotropins)

IT 60-92-4, CAMP
(induced by the use of PDE inhibitors; methods for the treatment of infertility with inhibitors of phosphodiesterases (PDE) in conjunction with gonadotropins)

IT 9036-21-9, Phosphodiesterase 4 9040-59-9, 3',5'-Cyclic nucleotide phosphodiesterase 9068-52-4, Phosphodiesterase 5
(inhibitors; methods for the treatment of infertility with inhibitors of phosphodiesterases (PDE) in conjunction with gonadotropins)

IT 58-32-2, Dipyridamole 58-74-2, Papaverine 37762-06-4, Zaprinast 42971-09-5, Vinpocetine 66327-51-3, Furazlocillin 131774-53-3, KS-505a 136145-07-8, Arofylline 139145-27-0 139755-83-2, Sildenafil 141184-34-1, Filaminast 144035-83-6, Piclamilast 147676-53-7 147676-63-9 150452-19-0 153259-65-5, Ariflo 162401-32-3, Roflumilast 162542-90-7, CDP840 167298-74-0, SCH-51866 170632-47-0, YC-1 171596-29-5, Tadalafil 178308-66-2, E-4010 184147-55-5 189940-24-7, Mesopram 191982-35-1 191982-37-3 191982-38-4 191982-52-2 215297-27-1, UK 343664 224157-99-7, Sch 59498 224785-90-4, Vardenafil 247568-68-9, FR226807 247580-98-9 247582-13-4 257892-34-5, D4418 319427-14-0, Bay-38-9456 334826-98-1, 5-[2-Ethoxy-5-(4-ethylpiperazin-1-ylsulfonyl)pyridin-3-yl]-3-ethyl-2-(2-methoxyethyl)-2,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one 334827-47-3 334827-59-7 335077-64-0 335077-70-8, 5-(5-Acetyl-2-butoxy-3-pyridinyl)-3-ethyl-2-(1-ethyl-3-azetidinyl)-2,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one 415916-46-0, Pharmaprojects 4516 415916-47-1, Pharmaprojects 5051 415916-49-3, Pharmaprojects 5064 415916-50-6, Pharmaprojects 5069 415916-57-3, E-8010 415916-78-8, Bay-38-3045 510719-07-0 663904-46-9 771524-82-4 773146-33-1, AWD 12-171 773146-41-1, AWD 12-217 773146-42-2, BMS

341400 773146-52-4, 5E3623 773146-54-6, 5E3569 773146-55-7, 5E3657
773146-78-4, Win 61691 773146-91-1, CL 1044
(methods for the treatment of infertility with inhibitors of phosphodiesterases (PDE) in conjunction with gonadotropins)

L15 ANSWER 2 OF 55 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:66518 CAPLUS
DOCUMENT NUMBER: 139:224597
TITLE: Ovarian stimulation by clomiphene citrate and hMG in combination with cetrorelix acetate for ICSI cycles
AUTHOR(S): Hwang, Jiann-Loung; Huang, Lee-Wen; Hsieh, Bih-Chwen; Tsai, Yieh-Loong; Huang, Shih-Chia; Chen, Chin-Yu; Hsieh, Mei-Ling; Chen, Pei-Hsin; Lin, Yu-Hung
CORPORATE SOURCE: Department of Obstetrics and Gynecology, Shin Kong Wu Ho-Su Memorial Hospital, Taipei, Taiwan
SOURCE: Human Reproduction (2003), 18(1), 45-49
CODEN: HUREEE; ISSN: 0268-1161
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB BACKGROUND: The introduction of GnRH antagonists such as cetrorelix acetate has made possible the simplification of ovarian stimulation. However, the most effective protocol for their administration has not yet been clearly defined. METHODS: Forty women with male-factor infertility undergoing 40 intracytoplasmic sperm injection (ICSI) cycles were included in the study. Clomiphene citrate at 100 mg a day was given from cycle day 3 through day 7. Human menopausal gonadotropin (hMG) at 150 IU was given on cycle days 4, 6 and 8, and was adjusted from day 9 according to the follicular and hormone responses. Cetrorelix acetate at 2.5 mg was administered when the leading follicle reached 14 mm. The remaining 0.5 mg was divided into two 0.25 mg injections for possible later use. Serum FSH, LH, estradiol and progesterone levels were measured daily from the day of cetrorelix acetate injection until hCG was given. RESULTS: Serum LH level was suppressed effectively for 4 days. Four patients (10%) needed one or two addnl. injections of 0.25 mg cetrorelix acetate. No premature LH surge was detected in any of the women treated. Sixteen women became pregnant (40%), of which 14 pregnancies (35%) were ongoing at the time of writing. CONCLUSIONS: This study demonstrates that this new protocol is feasible for couples with male-factor infertility undergoing ICSI.
IT Fertility
(female; ovarian stimulation by clomiphene citrate and gonadotropin in combination with cetrorelix acetate for intracytoplasmic sperm injection cycles)
IT Fertilization
(intracytoplasmic sperm injection; ovarian stimulation by clomiphene citrate and gonadotropin in combination with cetrorelix acetate for intracytoplasmic sperm injection cycles)
IT Human
Ovary
(ovarian stimulation by clomiphene citrate and gonadotropin in combination with cetrorelix acetate for intracytoplasmic sperm injection cycles)
IT 50-28-2, Estradiol, biological studies 57-83-0, Progesterone, biological studies 9002-61-3, Chorionic gonadotropin 9002-67-9, LH 9002-68-0, FSH
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(ovarian stimulation and hormone secretion response to clomiphene citrate and gonadotropin in combination

with cetrorelix acetate for intracytoplasmic sperm injection cycles)

IT 50-41-9, Clomiphene citrate 61489-71-2, Menopausal gonadotropin 145672-81-7, Cetrorelix acetate
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ovarian stimulation by clomiphene citrate and gonadotropin in combination with cetrorelix acetate for intracytoplasmic sperm injection cycles)

IT 50-41-9, Clomiphene citrate 145672-81-7, Cetrorelix acetate
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ovarian stimulation by clomiphene citrate and gonadotropin in combination with cetrorelix acetate for intracytoplasmic sperm injection cycles)

RN 50-41-9 CAPLUS

CN Ethanamine, 2-[4-(2-chloro-1,2-diphenylethenyl)phenoxy]-N,N-diethyl-, 2-hydroxy-1,2,3-propanetricarboxylate (1:1) (9CI) (CA INDEX NAME)

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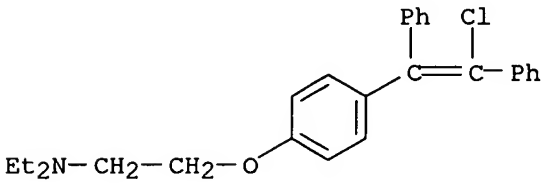

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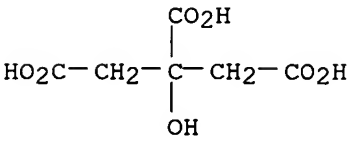

RN 145672-81-7 CAPLUS

CN D-Alaninamide, N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-D-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-L-tyrosyl-N5-(aminocarbonyl)-D-ornithyl-L-leucyl-L-arginyl-L-prolyl-, acetate (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 120287-85-6
CMF C70 H92 Cl N17 O14

Absolute stereochemistry.

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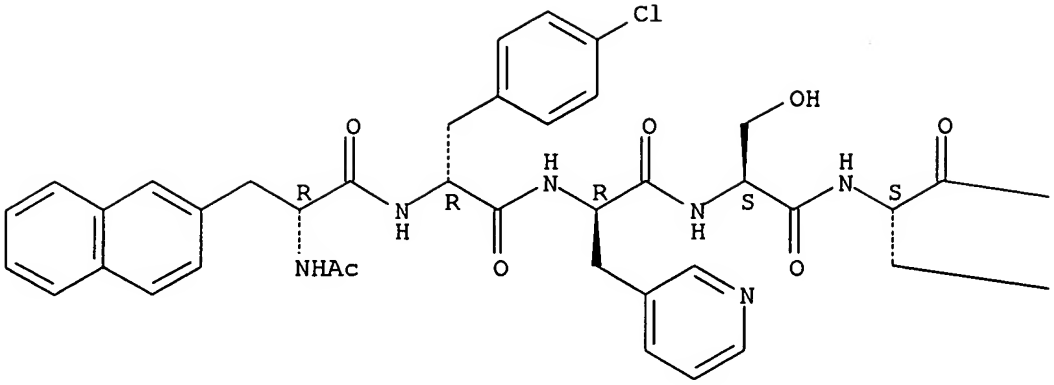

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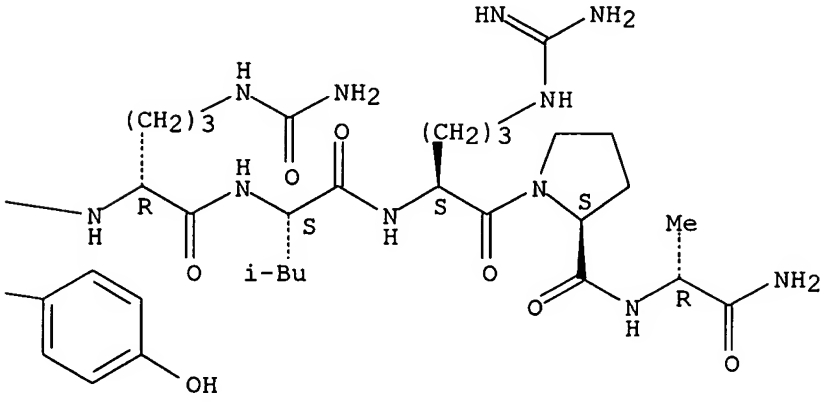
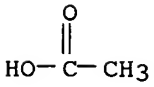


CM 2

CRN 64-19-7
CMF C2 H4 O2



REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 3 OF 55 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:502865 CAPLUS
DOCUMENT NUMBER: 135:339455
TITLE: Gonadotropin-releasing hormone antagonist protocol: a novel method of ovarian stimulation in poor responders
AUTHOR(S): Nikolettos, N.; Al-Hasani, S.; Felberbaum, R.; Demirel, L. C.; Kupker, W.; Montzka, P.; Xia, Y. X.; Schopper, B.; Sturm, R.; Diedrich, K.
CORPORATE SOURCE: Department of Obstetrics/Gynecology, Medical University Luebeck, Luebeck, D-23538, Germany

SOURCE: European Journal of Obstetrics & Gynecology and Reproductive Biology (2001), 97(2), 202-207
CODEN: EOGRAL; ISSN: 0301-2115
PUBLISHER: Elsevier Science Ireland Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The objective of the study was to estimate the efficacy of gonadotropin-releasing hormone (GnRH) antagonist ' Cetrorelix' in poor responders comparing with the standard long protocol. The study population consisted of 21 poor responders who underwent ICSI and treated with Cetrorelix according to the multiple-dose protocol and who were compared with 21 poor responders treated according to the long protocol and who also underwent ICSI. Patients in both groups were matched for chronol. age, the number of follicles found by ultrasound at the retrieval day and cause of infertility. Fifteen patients of GnRH antagonist group were treated with the combination of GnRH antagonist with clomiphene citrate (CC) plus gonadotropins, while six patients were treated with the combination of GnRH antagonist plus gonadotropins, but without CC. The use of GnRH antagonist in a multiple dose protocol gave a pregnancy rate of 14.28% which was in the range expected for patient with poor response, but with shorter treatment duration and with fewer ampoules of gonadotropins as compared with the use of a GnRH agonist protocol in a depot formulation. Within Cetrorelix group patients who received CC had a significant shorter duration of stimulation and needed fewer ampoules as compared with patients in the same group who did not receive CC. A GnRH antagonist multiple dose protocol may be the protocol of choice for the treatment of poor responders. The use of GnRH antagonist Cetrorelix ended with significantly less ampoules of gonadotropins and a shorter duration of stimulation.

IT Fertility
(female; gonadotropin-releasing hormone antagonist in relation to ovarian stimulation in poor responders in women)

IT Ovary
(follicle; gonadotropin-releasing hormone antagonist in relation to ovarian stimulation in poor responders in women)

IT Embryo, animal
Fertilization
Pregnancy
(gonadotropin-releasing hormone antagonist in relation to ovarian stimulation in poor responders in women)

IT Egg
(oocyte; gonadotropin-releasing hormone antagonist in relation to ovarian stimulation in poor responders in women)

IT 9002-61-3, Human chorionic gonadotropin
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(gonadotropin-releasing hormone antagonist in relation to ovarian stimulation in poor responders in women)

IT 57-83-0, Utrogestan, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(gonadotropin-releasing hormone antagonist in relation to ovarian stimulation in poor responders in women)

IT 50-41-9, Clomiphene citrate 57773-63-4 61489-71-2, Human menopausal gonadotropin 120287-85-6, Cetrorelix
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(gonadotropin-releasing hormone antagonist in relation to

ovarian stimulation in poor responders in women)

IT 50-28-2, Estradiol, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(gonadotropin-releasing hormone antagonist in relation to ovarian stimulation in poor responders in women)

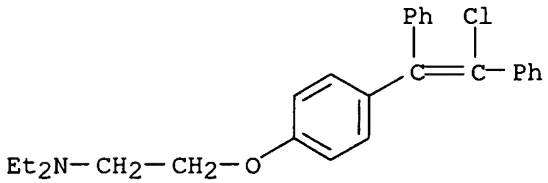
IT 50-41-9, Clomiphene citrate 120287-85-6, Cetrorelix
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(gonadotropin-releasing hormone antagonist in relation to ovarian stimulation in poor responders in women)

RN 50-41-9 CAPLUS

CN Ethanamine, 2-[4-(2-chloro-1,2-diphenylethenyl)phenoxy]-N,N-diethyl-, 2-hydroxy-1,2,3-propanetricarboxylate (1:1) (9CI) (CA INDEX NAME)

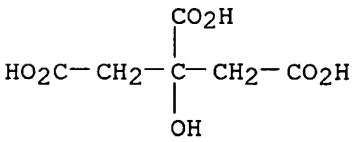
CM 1

CRN 911-45-5
CMF C26 H28 Cl N O



CM 2

CRN 77-92-9
CMF C6 H8 O7

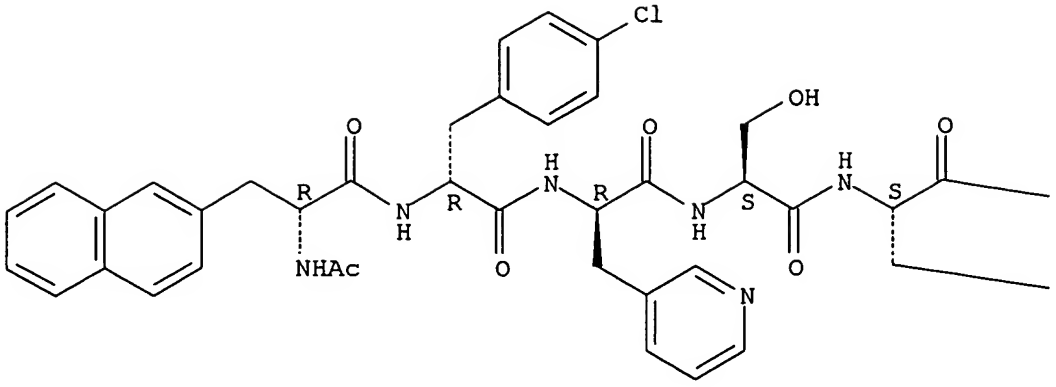


RN 120287-85-6 CAPLUS

CN D-Alaninamide, N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-D-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-L-tyrosyl-N5-(aminocarbonyl)-D-ornithyl-L-leucyl-L-arginyl-L-prolyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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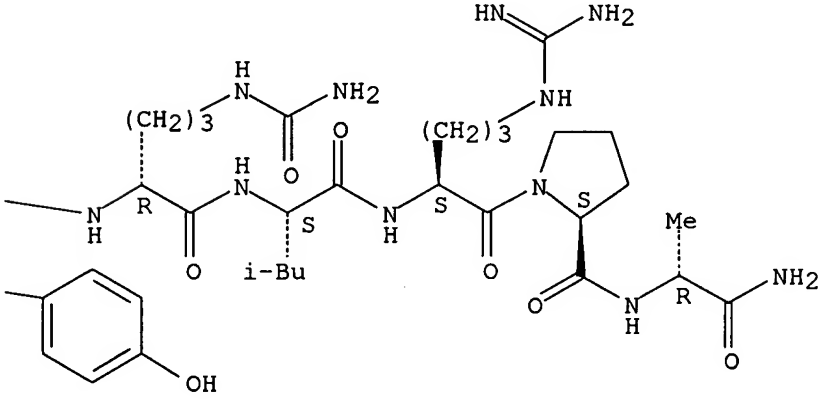


REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 4 OF 55 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:700864 CAPLUS
DOCUMENT NUMBER: 139:391470
TITLE: Single dose application of cetrorelix in combination with clomiphene for friendly IVF: results of a feasibility study
AUTHOR(S): Engel, J. B.; Olivennes, F.; Fanchin, R.; Frydman, N.; Le Du, A.; Blanchet, V.; Frydman, R.
CORPORATE SOURCE: Department of Obstetrics and Gynecology, Hopital Antoine Beclere, Clamart, 92141, Fr.
SOURCE: Reproductive BioMedicine Online (2003), 6(4), 444-447
CODEN: RBOEA6; ISSN: 1472-6483
PUBLISHER: Reproductive Healthcare Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A prospective randomized feasibility study was carried out on 10 patients undergoing IVF treatment using a single-dose LHRH antagonist protocol (cetrorelix, Cetrotide) with clomiphene citrate in combination with either human menopausal gonadotrophin (HMG) or recombinant human FSH (rFSH). Both treatment-groups, HMG and rFSH, were comparable with regard to age (33.2 vs. 34,4 yr) BMI (23.2 vs. 22.7) and cause of infertility. They yielded comparable results concerning gonadotrophin dose (19.8 vs. 17.0),

stimulation days (6.5 vs. 8) and live births (one vs. two). No premature LH surge (LH >10 IU/mL and progesterone >1 ng/mL) occurred. The overall baby take-home rate was 30%. In a small number of patients, cetrorelix could be shown to effectively prevent premature LH surges in stimulation protocols combining clomiphene with gonadotrophins with an excellent baby take-home rate per started cycle of 30%.

IT Fertility
(female; single dose application of cetrorelix in combination with clomiphene and gonadotropins for friendly IVF)

IT Newborn
(outcome; single dose application of cetrorelix in combination with clomiphene and gonadotropins for friendly IVF)

IT Human
In vitro fertilization
Ovulation induction
(single dose application of cetrorelix in combination with clomiphene and gonadotropins for friendly IVF)

IT 57-83-0, Progesterone, biological studies 9002-67-9, LH
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(hormone response to single dose application of cetrorelix in combination with clomiphene and gonadotropins for friendly IVF)

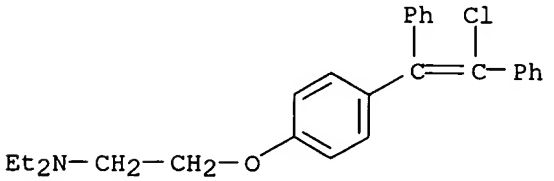
IT 146479-72-3, Gonal F
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(recombinant human; single dose application of cetrorelix in combination with clomiphene and gonadotropins for friendly IVF)

IT 911-45-5, Clomiphene 9034-40-6D, LH-RH, antagonist analogs 61489-71-2, Menogon 145672-81-7, Cetrotide
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(single dose application of cetrorelix in combination with clomiphene and gonadotropins for friendly IVF)

IT 911-45-5, Clomiphene 145672-81-7, Cetrotide
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(single dose application of cetrorelix in combination with clomiphene and gonadotropins for friendly IVF)

RN 911-45-5 CAPLUS

CN Ethanamine, 2-[4-(2-chloro-1,2-diphenylethenyl)phenoxy]-N,N-diethyl- (9CI) (CA INDEX NAME)



RN 145672-81-7 CAPLUS

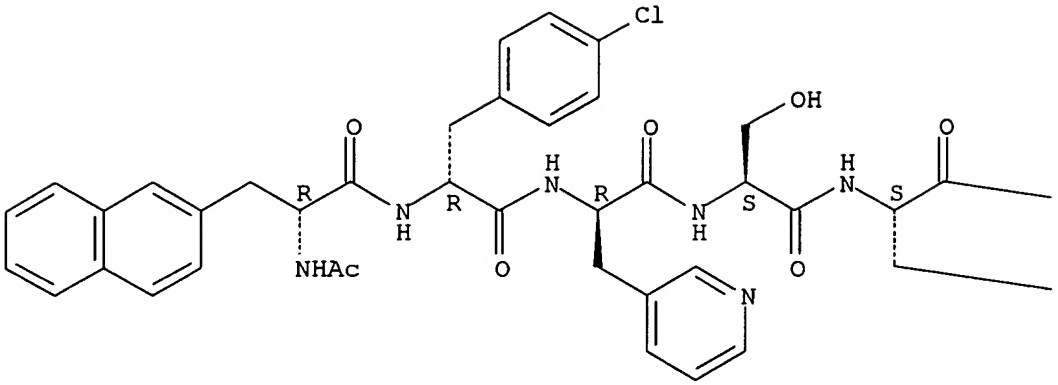
CN D-Alaninamide, N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-D-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-L-tyrosyl-N5-(aminocarbonyl)-D-ornithyl-L-leucyl-L-arginyl-L-prolyl-, acetate (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 120287-85-6
CMF C70 H92 Cl N17 O14

Absolute stereochemistry.

PAGE 1-A



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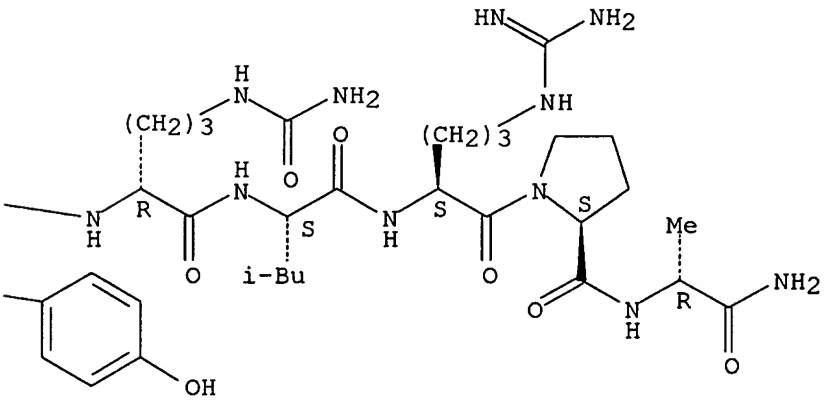

CM 2

CRN 64-19-7
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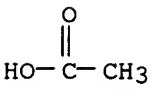


REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 5 OF 55 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:700862 CAPLUS
DOCUMENT NUMBER: 139:271177
TITLE: The impact of LH serum concentration on the clinical outcome of IVF cycles in patients receiving two regimens of clomiphene

citrate/gonadotrophin/0.25 mg cetrorelix

AUTHOR(S): Tavaniotou, Asimina; Albano, Carola; Van Steirteghem, Andre; Devroey, Paul
CORPORATE SOURCE: AZ-VUB, Centre for Reproductive Medicine, Dutch-Speaking Free University of Brussels, Brussels, 1090, Belg.

SOURCE: Reproductive BioMedicine Online (2003), 6(4), 421-426
CODEN: RBOEA6; ISSN: 1472-6483
PUBLISHER: Reproductive Healthcare Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Clomiphene citrate treatment with the association of gonadotrophins and the GnRH antagonist cetrorelix 0.25mg was analyzed in two different stimulation protocols for IVF. In protocol 1, 18 patients were sequentially stimulated with clomiphene citrate and gonadotrophins. In protocol 11, 28 patients started the gonadotrophin injections during the clomiphene citrate administration. LH values significantly dropped after the first 0.25 mg cetrorelix injection in both protocols. A total of 22% and 7% of cycles were cancelled in protocols I and II, resp., because of poor follicular development. The clin. pregnancy rate following embryo transfer was 18.1% in protocol I and 29.1% in protocol II. In two (11.1%) cycles stimulated according to protocol I and in eight (28.5%) cycles from protocol II, premature LH surges occurred. In patients with premature LH surge, significantly fewer metaphase II oocytes were obtained. The clin. pregnancy rate following embryo transfer was 12.5% in patients with surge compared with 29.6% in patients without LH values were lower before HCG injection in patients who achieved pregnancy in the study cycle. In conclusion, sequential clomiphene citrate and gonadotrophin administration is not recommended for clomiphene citrate/gonadotrophin/cetrorelix 0.25 cycles.
Cetrorelix 0.25 mg/day was associated with a high incidence of premature LH surges and premature LH surges were associated with an adverse cycle outcome.

IT Ovary
(follicle; impact of clomiphene citrate/gonadotrophin/cetrorelix on LH serum and in vitro fertilization outcome)

IT Human
In vitro fertilization
Pregnancy
(impact of clomiphene citrate/gonadotrophin/cetrorelix on LH serum and in vitro fertilization outcome)

IT Gonadotropins
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(impact of clomiphene citrate/gonadotrophin/cetrorelix on LH serum and in vitro fertilization outcome)

IT 9034-40-6, GnRH
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(antagonist; impact of clomiphene citrate/gonadotrophin/cetrorelix on LH serum and in vitro fertilization outcome)

IT 120287-85-6, Cetrorelix
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(impact of clomiphene citrate/gonadotrophin/cetrorelix on LH serum and in vitro fertilization outcome)

IT 9002-67-9, LH
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(impact of clomiphene citrate/gonadotrophin/cetrorelix on LH serum and in vitro fertilization outcome)

IT 50-41-9, Clomiphene citrate
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(impact of clomiphene citrate/gonadotrophin/
cetrorelix on LH serum and in vitro fertilization outcome)

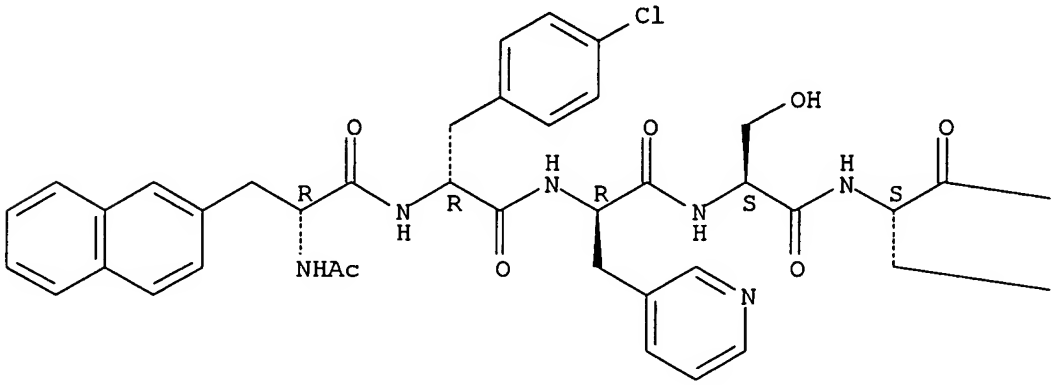
IT 120287-85-6, Cetrorelix
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(impact of clomiphene citrate/gonadotrophin/
cetrorelix on LH serum and in vitro fertilization outcome)

RN 120287-85-6 CAPLUS

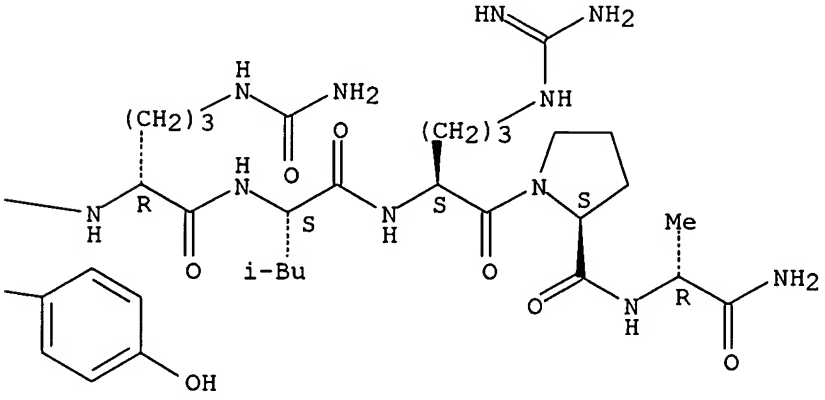
CN D-Alaninamide, N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-D-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-L-tyrosyl-N5-(aminocarbonyl)-D-ornithyl-L-leucyl-L-arginyl-L-prolyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



IT 50-41-9, Clomiphene citrate
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(impact of clomiphene citrate/gonadotrophin/
cetrorelix on LH serum and in vitro fertilization outcome)

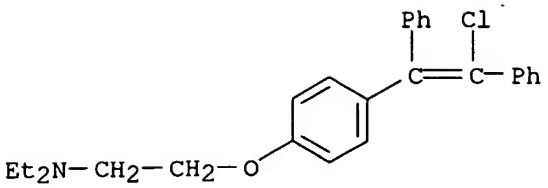
RN 50-41-9 CAPLUS

CN Ethanamine, 2-[4-(2-chloro-1,2-diphenylethenyl)phenoxy]-N,N-diethyl-, 2-hydroxy-1,2,3-propanetricarboxylate (1:1) (9CI) (CA INDEX NAME)

CM 1

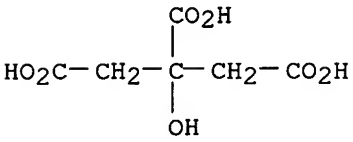
CRN 911-45-5

CMF C26 H28 Cl N O



CM 2

CRN 77-92-9
CMF C6 H8 O7



REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 6 OF 55 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2006:616216 CAPLUS
TITLE: Comparison of outcome of clomiphene citrate/human menopausal gonadotropin/ cetrorelix protocol and buserelin long protocol - a randomized study
AUTHOR(S): Tzeng, Chi-Ruey; Lin, Yu-Hung; Hwang, Jiann-Loung; Seow, Kok-Min; Huang, Lee-Wen; Hsieh, Bih-Chwen
CORPORATE SOURCE: Dept. of Obstetrics and Gynecology, Shin Kong Wu Ho-Su Memorial Hospital, Taipei, Taiwan
SOURCE: Gynecological Endocrinology (2006), 22(6), 297-302
CODEN: GYENER; ISSN: 0951-3590
PUBLISHER: Taylor & Francis Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB This study evaluates the efficacy of a stimulation protocol with clomiphene citrate (CC)/human menopausal gonadotropin (hMG)/cetrorelix and its effects on oocyte quality and endometrium. One hundred and twenty couples with male-factor infertility who were about to undergo their first intracytoplasmic sperm injection cycles were randomized into two groups. Sixty women were stimulated with the CC/hMG/cetrorelix protocol (cetrorelix group) and 60 received the buserelin long protocol (buserelin group). Fewer oocytes were recovered in the cetrorelix group than in the buserelin group (mean ± standard deviation (SD): 11.1 ± 4.0 vs. 17.3 ± 5.8, $p < 0.001$); however, the percentages of metaphase II, metaphase I and germinal vesicle oocytes were similar between the two groups. Serum estradiol level was significantly lower in the cetrorelix than in the buserelin group (mean ± SD: 2600.58 ± 1189.11 vs. 3293.46 ± 1221.49 pg/mL, $p = 0.006$), but the endometrial thickness was similar. The implantation rates (19.2% vs. 17.7%) and the pregnancy rates (41.7% vs. 40.0%) were similar between groups. The ampoules (mean ± SD: 18.9 ± 3.0 vs. 38.9 ± 12.2, $p < 0.001$) and injections (mean ± SD: 6.8 ± 1.1 vs. 15.7 ± 3.1, $p < 0.001$) of gonadotropin used were significantly lower in

the cetrorelix group than in the buserelin group. No patients in either group developed a premature LH surge. The present study found no statistically significant difference between the two treatment modalities with regard to pregnancy rates.

REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 7 OF 55 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:666550 CAPLUS

DOCUMENT NUMBER: 138:19649

TITLE: Use of cetrorelix in combination with clomiphene citrate and gonadotrophins: a suitable approach to friendly IVF?

AUTHOR(S): Engel, J. B.; Ludwig, M.; Felberbaum, R.; Albano, C.; Devroey, P.; Diedrich, K.

CORPORATE SOURCE: Department of Gynecology and Obstetrics, Division of Reproductive Medicine and Gynecologic Endocrinology, University Clinic, Luebeck, 23538, Germany

SOURCE: Human Reproduction (2002), 17(8), 2022-2026
CODEN: HUREEE; ISSN: 0268-1161

PUBLISHER: Oxford University Press

DOCUMENT TYPE: Journal

LANGUAGE: English

AB BACKGROUND: With the recently introduced GnRH antagonists, soft stimulation protocols on the basis of clomiphene pretreatment should be possible as the pituitary remains fully sensitive at the beginning of the cycle. METHODS: A prospective trial was carried out on 107 patients undergoing IVF treatment using the multiple dose GnRH antagonist protocol (cetrorelix), clomiphene citrate, and either HMG (n = 54) or recombinant FSH (rFSH) (n = 53). Different stimulation protocols were used to find the most appropriate one for clin. application. RESULTS: Both treatment groups, HMG and rFSH, yielded comparable results concerning gonadotrophin dose, stimulation days and pregnancy rate. A mean number of 6.34±4.4 metaphase II oocytes was retrieved and a mean number of 2.45±0.65 embryos was transferred. However, the overall rate of premature LH surges was 21.5% (defined as measurement of LH >10 IU/l and progesterone >1 ng/mL) which is unacceptable for clin. practice. CONCLUSIONS: Increasing the daily cetrorelix dose from 0.25 to 0.5 mg might decrease the number of premature LH surges. Soft stimulation protocols with clomiphene should be used cautiously.

IT Pregnancy
(rate; use of cetrorelix in combination with clomiphene citrate and gonadotrophins as a suitable approach to friendly IVF)

IT Ovary
(stimulation; use of cetrorelix in combination with clomiphene citrate and gonadotrophins as a suitable approach to friendly IVF)

IT Human
In vitro fertilization
(use of cetrorelix in combination with clomiphene citrate and gonadotrophins as a suitable approach to friendly IVF)

IT 9002-67-9, Luteinizing hormone
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(number of premature LH surges; use of cetrorelix in combination with clomiphene citrate and gonadotrophins as a suitable approach to friendly IVF)

IT 50-41-9, Clomiphene citrate 61489-71-2, Menogon 145672-81-7, Cetrotide 146479-72-3, Gonal F
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(use of cetrorelix in combination with clomiphene

citrate and gonadotrophins as a suitable approach to friendly IVF)

IT 50-41-9, Clomiphene citrate 145672-81-7, Cetrotide
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(use of cetrorelix in combination with clomiphene citrate and gonadotrophins as a suitable approach to friendly IVF)

RN 50-41-9 CAPLUS

CN Ethanamine, 2-[4-(2-chloro-1,2-diphenylethenyl)phenoxy]-N,N-diethyl-, 2-hydroxy-1,2,3-propanetricarboxylate (1:1) (9CI) (CA INDEX NAME)

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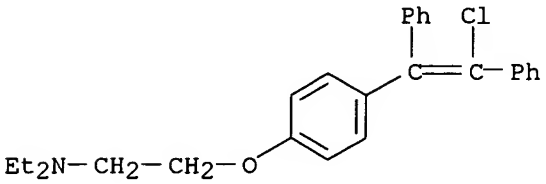
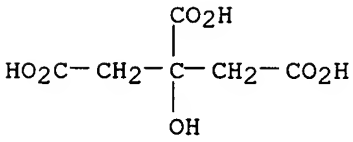
CRN 911-45-5
CMF C26 H28 Cl N O



CM 2

CRN 77-92-9
CMF C6 H8 O7



RN 145672-81-7 CAPLUS

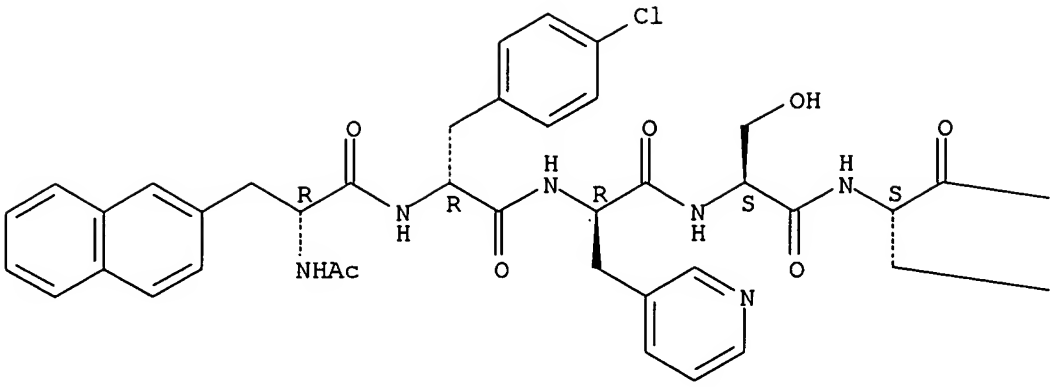
CN D-Alaninamide, N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-D-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-L-tyrosyl-N5-(aminocarbonyl)-D-ornithyl-L-leucyl-L-arginyl-L-prolyl-, acetate (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 120287-85-6
CMF C70 H92 Cl N17 O14

Absolute stereochemistry.

PAGE 1-A



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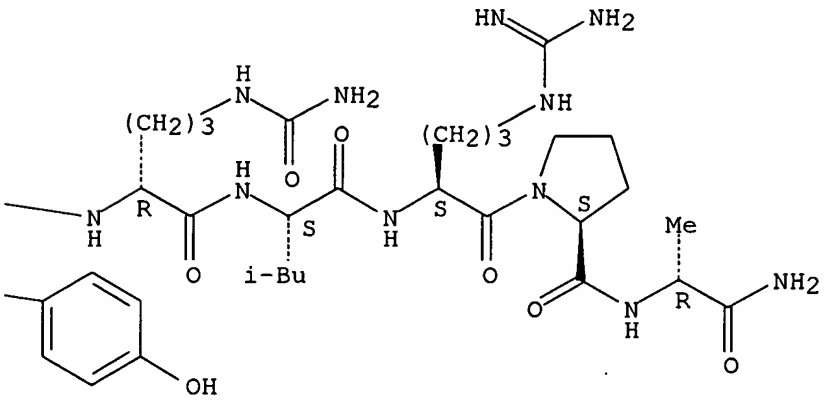

CM 2

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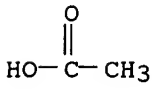
CMF C2 H4 O2



REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 8 OF 55 USPATFULL on STN
ACCESSION NUMBER: 2005:98574 USPATFULL
TITLE: Methods of preventing or treating disorders by administering and integrin alphanubeta3 antagonist in combination with an HMG-CoA reductase inhibitor or a bisphosphonate
INVENTOR(S): Wilder, Ronald L., Derwood, MD, UNITED STATES
Mao, Su-Yau, Gaithersburg, MD, UNITED STATES

NUMBER	KIND	DATE

PATENT INFORMATION: US 2005084489 A1 20050421
APPLICATION INFO.: US 2003-379145 A1 20030304 (10)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2002-361859P	20020304 (60)
	US 2002-370398P	20020405 (60)
	US 2003-444265P	20030130 (60)
	US 2003-444156P	20030130 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: JOHNATHAN KLEIN-EVANS, ONE MEDIMMUNE WAY, GAITHERSBURG, MD, 20878, US
NUMBER OF CLAIMS: 27
EXEMPLARY CLAIM: 1
LINE COUNT: 6785
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention provides methods of preventing, treating, managing or ameliorating disorders utilizing an integrin α.sub.vβ.sub.3 antagonist in combination with an HMG -CoA reductase inhibitor and/or a bisphosphonate. The present invention also encompasses methods of preventing, treating, managing or ameliorating disorders utilizing an integrin α.sub.vβ.sub.3 antagonist in combination with an HMG-CoA reductase inhibitor and/or a bisphophonate, in further combination with another therapy (e.g., another prophylactic or therapeutic agent or treatment) which is not an integrin α.sub.vβ.sub.3 antagonist, an HMG -CoA reductase inhibitor, or a bisphosphonate. In particular, the present invention provides methods of preventing, treating, managing or ameliorating inflammatory diseases, autoimmune disorders, disorders associated with aberrant expression and/or activity of integrin α.sub.vβ.sub.3, disorders associated with abnormal bone metabolism, disorders associated with aberrant angiogenesis and cancers, or conditions associated therewith, utilizing an antibody that immunospecifically binds to integrin α.sub.vβ.sub.3 (e.g., VITAXIN®) in combination with an HMG-CoA reductase inhibitor and/or bisphosphonate, and optionally in combination with another therapy (e.g., another prophylactic or therapeutic agent or treatment) which is not an integrin α.sub.vβ.sub.3 antagonist, an HMG-CoA reductase inhibitor, or a bisphosphonate. The present also invention encompasses compositions and articles of manufacture for use in preventing, treating, managing or ameliorating inflammatory diseases, autoimmune disorders, disorders associated with aberrant expression and/or activity of integrin α.sub.vβ.sub.3, disorders associated with abnormal bone metabolism, disorders associated with aberrant angiogenesis and cancers, or conditions associated therewith.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT Inflammation
(Crohn's disease; preventing or treating disorders by administering an integrin αvβ3 antagonist in combination with an HMG-CoA reductase inhibitor or a bisphosphonate or other therapeutic agent)
IT Intestine, disease
(Crohn's; preventing or treating disorders by administering an integrin αvβ3 antagonist in combination with an HMG-CoA reductase inhibitor or a bisphosphonate or other therapeutic agent)
IT Bone, disease
(Gorham-Stout disease; preventing or treating disorders by administering an integrin αvβ3 antagonist in combination with an HMG-CoA reductase inhibitor or a bisphosphonate or other therapeutic agent)
IT Bone, disease

(Paget's; preventing or treating disorders by administering an integrin αvβ3 antagonist in combination with an HMG-CoA reductase inhibitor or a bisphosphonate or other therapeutic agent)

IT Angiogenesis
(aberrant; preventing or treating disorders by administering an integrin αvβ3 antagonist in combination with an HMG-CoA reductase inhibitor or a bisphosphonate or other therapeutic agent)

IT Antibodies and Immunoglobulins
(anti-integrin αvβ3; preventing or treating disorders by administering an integrin αvβ3 antagonist in combination with an HMG-CoA reductase inhibitor or a bisphosphonate or other therapeutic agent)

IT Antiarteriosclerotics
(antiatherosclerotics; preventing or treating disorders by administering an integrin αvβ3 antagonist in combination with an HMG-CoA reductase inhibitor or a bisphosphonate or other therapeutic agent)

IT Disease, animal
(arthropathy, aseptic loosening of replacement; preventing or treating disorders by administering an integrin αvβ3 antagonist in combination with an HMG-CoA reductase inhibitor or a bisphosphonate or other therapeutic agent)

IT Intestine, neoplasm
(colon; preventing or treating disorders by administering an integrin αvβ3 antagonist in combination with an HMG-CoA reductase inhibitor or a bisphosphonate or other therapeutic agent)

IT Eye, disease
(diabetic retinopathy; preventing or treating disorders by administering an integrin αvβ3 antagonist in combination with an HMG-CoA reductase inhibitor or a bisphosphonate or other therapeutic agent)

IT Joint, anatomical
(disease, aseptic loosening of replacement; preventing or treating disorders by administering an integrin αvβ3 antagonist in combination with an HMG-CoA reductase inhibitor or a bisphosphonate or other therapeutic agent)

IT Eye, disease
(macula, degeneration; preventing or treating disorders by administering an integrin αvβ3 antagonist in combination with an HMG-CoA reductase inhibitor or a bisphosphonate or other therapeutic agent)

IT Bone, neoplasm
(metastasis; preventing or treating disorders by administering an integrin αvβ3 antagonist in combination with an HMG-CoA reductase inhibitor or a bisphosphonate or other therapeutic agent)

IT Estrogen receptors
(modulators; preventing or treating disorders by administering an integrin αvβ3 antagonist in combination with an HMG-CoA reductase inhibitor or a bisphosphonate or other therapeutic agent)

IT Bone, disease
(osteolysis, inflammatory; preventing or treating disorders by administering an integrin αvβ3 antagonist in combination with an HMG-CoA reductase inhibitor or a bisphosphonate or other therapeutic agent)

IT Bone, disease
(osteopenia; preventing or treating disorders by administering an integrin αvβ3 antagonist in combination with an HMG-CoA reductase inhibitor or a bisphosphonate or other therapeutic agent)

IT Angiogenesis inhibitors

IT Anti-inflammatory agents

IT Antiarthritics

IT Antirheumatic agents

IT Antitumor agents

IT Arthritis
IT Atherosclerosis
IT Autoimmune disease
IT Behcet's syndrome
IT Bone, neoplasm
IT Drug interactions
IT Human
IT Immunomodulators
IT Inflammation
IT Lung, neoplasm
IT Mammary gland, neoplasm
IT Melanoma
IT Neoplasm
IT Osteoarthritis
IT Osteoporosis
IT Ovary, neoplasm
IT Periodontium, disease
IT Prostate gland, neoplasm
IT Radiotherapy
IT Rheumatoid arthritis
(preventing or treating disorders by administering an integrin αvβ3 antagonist in combination with an HMG-CoA reductase inhibitor or a bisphosphonate or other therapeutic agent)
IT Estrogens
(preventing or treating disorders by administering an integrin αvβ3 antagonist in combination with an HMG-CoA reductase inhibitor or a bisphosphonate or other therapeutic agent)
IT Artery, disease
(restenosis; preventing or treating disorders by administering an integrin αvβ3 antagonist in combination with an HMG-CoA reductase inhibitor or a bisphosphonate or other therapeutic agent)
IT Integrins
(αvβ3; preventing or treating disorders by administering an integrin αvβ3 antagonist in combination with an HMG-CoA reductase inhibitor or a bisphosphonate or other therapeutic agent)
IT 9028-35-7, 3-Hydroxy-3-methylglutaryl CoA reductase
(HMG-CoA reductase; preventing or treating disorders by administering an integrin αvβ3 antagonist in combination with an HMG-CoA reductase inhibitor or a bisphosphonate or other therapeutic agent)
IT 153377-38-9, GenBank L28832
(methods of preventing or treating disorders by administering an integrin αvβ3 antagonist in combination with an HMG-CoA reductase inhibitor or a bisphosphonate)
IT 1406-16-2, Vitamin D 9007-12-9, Calcitonin 13598-36-2D, Phosphonic acid, alkylidenebis- derivs. 324740-00-3, VITAXIN
(preventing or treating disorders by administering an integrin αvβ3 antagonist in combination with an HMG-CoA reductase inhibitor or a bisphosphonate or other therapeutic agent)
IT 162290-66-6 211373-80-7 315667-90-4 315667-92-6 459123-09-2 459123-10-5
(unclaimed sequence; methods of preventing or treating disorders by administering an integrin αvβ3 antagonist in combination with an HMG-CoA reductase inhibitor or a bisphosphonate)

L15 ANSWER 9 OF 55 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:214874 CAPLUS
DOCUMENT NUMBER: 143:1418
TITLE: A novel protocol of ovulation induction with delayed gonadotropin-releasing hormone antagonist administration combined with high-dose recombinant follicle-stimulating hormone and clomiphene citrate for poor responders and women over 35 years
AUTHOR(S): D'Amato, Giuseppe; Caroppo, Ettore; Pasquadibisceglie,

Annamaria; Carone, Domenico; Vitti, Angela; Vizziello, Giovanni Michele
CORPORATE SOURCE: Unita Operativa di Fisiopatologia della Riproduzione Umana, IRCCS "S. De Bellis", Castellana Grotte, Italy
SOURCE: Fertility and Sterility (2004), 81(6), 1572-1577
CODEN: FESTAS; ISSN: 0015-0282
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Objective: To evaluate the efficacy of a novel protocol of ovulation induction for poor responders. Design: Prospective, controlled, clin. study. Setting: Research institute's reproductive unit. Patient(s): One hundred forty-five infertile women, aged 27-39 years, candidates for assisted reproductive techniques (ART). Intervention(s): Before undergoing ART, 85 patients received clomiphene citrate, high-dose recombinant human FSH, and a delayed, multidose GnRH antagonist, whereas 60 patients underwent a standard long protocol. Main Outcome Measure(s): Estradiol levels (pg/mL), cancellation rate, oocyte retrieval, embryo score, and fertilization and pregnancy rates. Result(s): Patients undergoing the study protocol obtained lower cancellation rates (4.7% vs. 34%) and higher E2 levels (945.88 ± 173.2 pg/mL vs. 169.55 ± 45.07 pg/mL), oocyte retrieval (5.56 ± 1.13 vs. 3.36 ± 1.3), and pregnancy (22.2% vs. 15.3%) and implantation rates (13.5% vs. 7.6%) compared with those receiving the long protocol. Age neg. correlated with ovarian response in the latter, whereas the ovarian outcome results were comparable in younger (<35 yrs) and older (>35 yrs) women treated with the study protocol. Conclusion(s): The proposed protocol of ovulation induction can be usefully administered in poor responders as well as in aged woman, probably because the delayed administration of GnRH antagonist prevents its adverse effects on ovarian paracrine activity and on oocyte maturation.
IT Fertility disorders
(female; ovulation induction with delayed gonadotropin -releasing hormone antagonist combined with recombinant FSH and clomiphene citrate for poor responders and women over 35 yr)
IT Egg
(oocyte; ovulation induction with delayed gonadotropin -releasing hormone antagonist combined with recombinant FSH and clomiphene citrate for poor responders and women over 35 yr)
IT Aging, animal
Combination chemotherapy
Fertilization
Human
Ovulation induction
Reproduction disorders
(ovulation induction with delayed gonadotropin-releasing hormone antagonist combined with recombinant FSH and clomiphene citrate for poor responders and women over 35 yr)
IT 9034-40-6, Gonadotropin-releasing hormone
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(antagonist; ovulation induction with delayed gonadotropin -releasing hormone antagonist combined with recombinant FSH and clomiphene citrate for poor responders and women over 35 yr)
IT 50-41-9, Serophene 74381-53-6, Enantone 145672-81-7, Cetrotide 146479-72-3, Gonal F
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ovulation induction with delayed gonadotropin-releasing hormone antagonist combined with recombinant FSH and clomiphene citrate for poor responders and women over 35 yr)

IT 9002-61-3, Profasi
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ovulation induction with delayed gonadotropin-releasing hormone antagonist combined with recombinant FSH and clomiphene citrate for poor responders and women over 35 yr)

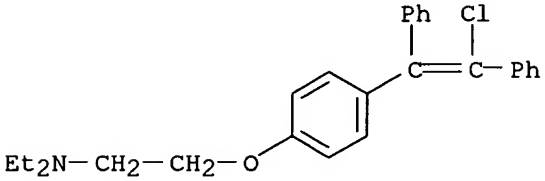
IT 50-41-9, Serophene 145672-81-7, Cetrotide
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ovulation induction with delayed gonadotropin-releasing hormone antagonist combined with recombinant FSH and clomiphene citrate for poor responders and women over 35 yr)

RN 50-41-9 CAPLUS

CN Ethanamine, 2-[4-(2-chloro-1,2-diphenylethenyl)phenoxy]-N,N-diethyl-, 2-hydroxy-1,2,3-propanetricarboxylate (1:1) (9CI) (CA INDEX NAME)

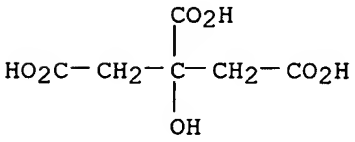
CM 1

CRN 911-45-5
CMF C26 H28 Cl N O



CM 2

CRN 77-92-9
CMF C6 H8 O7



RN 145672-81-7 CAPLUS

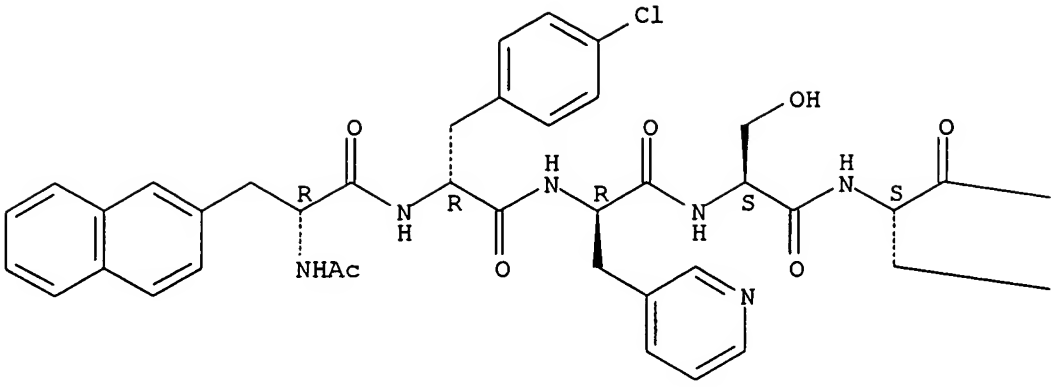
CN D-Alaninamide, N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-D-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-L-tyrosyl-N5-(aminocarbonyl)-D-ornithyl-L-leucyl-L-arginyl-L-prolyl-, acetate (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 120287-85-6
CMF C70 H92 Cl N17 O14

Absolute stereochemistry.

PAGE 1-A



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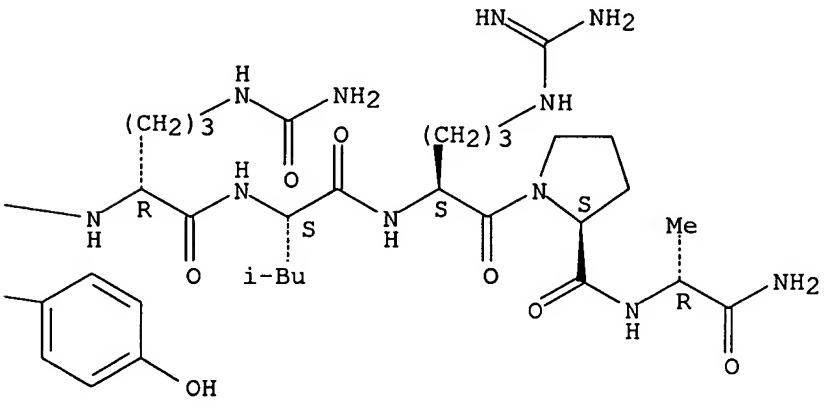
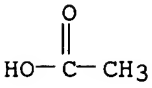


CM 2

CRN 64-19-7
CMF C2 H4 O2



REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 10 OF 55 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:182426 CAPLUS
DOCUMENT NUMBER: 142:233845
TITLE: LHRH-antagonists in the treatment of fertility disorders
INVENTOR(S): Bouchard, Philippe; Frydman, Rene; Devroey, Paul; Diedrich, Klaus; Engel, Jurgen
PATENT ASSIGNEE(S): Fr.
SOURCE: U.S. Pat. Appl. Publ., 7 pp., Cont. of U.S. Ser. No. 786,937.
CODEN: USXXCO

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2005049200	A1	20050303	US 2003-661780		20030915
PRIORITY APPLN. INFO.:			US 1996-11282P	P	19960207
			US 1997-786937	B2	19970122

AB A method of treating infertility disorders by (1) administering an LH-RH antagonist, preferably Cetrorelix, in amts. to selectively suppress endogenous LH but not FSH secretion and (2) inducing follicle growth by administration of exogenous gonadotropin. The selective suppression OF LH allows FSH secretion to be at natural levels thereby not affecting individual estrogen development. The LH-RH antagonist can be given as a single or dual s.c. dose in the range of 1 mg to 10 mg, preferably 2 mg-6 mg. In multiple dosing-posol., LH-RH antagonist can be administered s.c. in an amount in the range of 0.1 to 0.5 mg of LH-RH antagonist/day. LH-RH antagonist is applied starting cycle day 1 to 10, preferably on day 4 to 8, and ovulation can be induced between day 9 and 20 of the menstruation cycle by administering rec. LH, native LH-RH, LH-RH agonist or by HCG. In addition rec. LH, native LH-RH or LH-RH agonist can be given to avoid hyperstimulation syndrome and native LH-RH or a LH-RH agonist can be administered to avoid luteal phase stimulation by neutralizing the neg. effects of HCG.

IT Reproduction, animal
(ART (assisted reproductive techniques); LHRH-antagonists in treatment of fertility disorders)

IT Fertility disorders
Human
Ovulation induction
(LHRH-antagonists in treatment of fertility disorders)

IT Combination chemotherapy
(combination therapy with GnRH antagonist, clomifen citrate, and gonadotropins; LHRH-antagonists in treatment of fertility disorders)

IT Gonadotropins
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination therapy with GnRH antagonist, clomifen citrate, and gonadotropins; LHRH-antagonists in treatment of fertility disorders)

IT Antiestrogens
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination therapy with GnRH antagonist, clomifen citrate, and gonadotropins; LHRH-antagonists in treatment of fertility disorders)

IT Ovary
(follicle, induction of follicle growth; LHRH-antagonists in treatment of fertility disorders)

IT 9034-40-6, LH-RH
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(LHRH-antagonists in treatment of fertility disorders)

IT 120287-85-6, Cetrorelix 145672-81-7, Cetrorelix Acetate
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(LHRH-antagonists in treatment of fertility disorders)

IT 9002-67-9, Luteinizing hormone 9002-68-0, FSH
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity);

THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination therapy with GnRH antagonist, clomifen citrate, and gonadotropins; LHRH-antagonists in treatment of fertility disorders)

IT 50-41-9, Clomiphene citrate 911-45-5, Clomiphene 61489-71-2, Human menopausal gonadotropin
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination therapy with GnRH antagonist, clomifen citrate, and gonadotropins; LHRH-antagonists in treatment of fertility disorders)

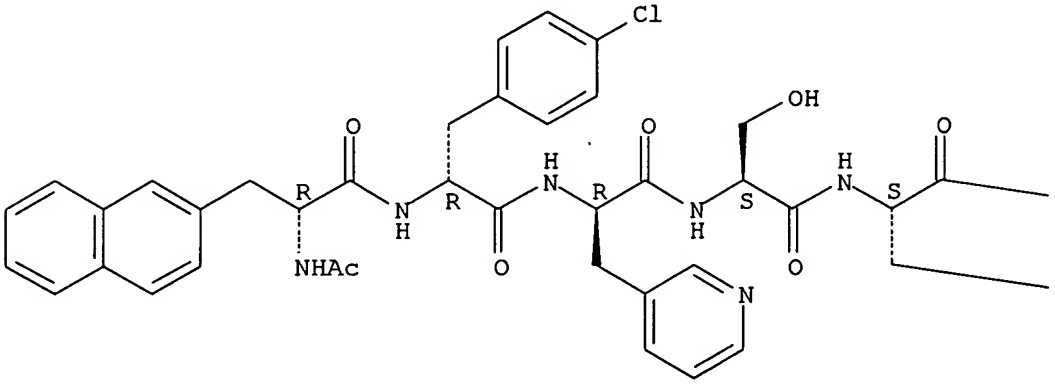
IT 120287-85-6, Cetrorelix 145672-81-7, Cetrorelix Acetate
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(LHRH-antagonists in treatment of fertility disorders)

RN 120287-85-6 CAPLUS

CN D-Alaninamide, N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-D-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-L-tyrosyl-N5-(aminocarbonyl)-D-ornithyl-L-leucyl-L-arginyl-L-prolyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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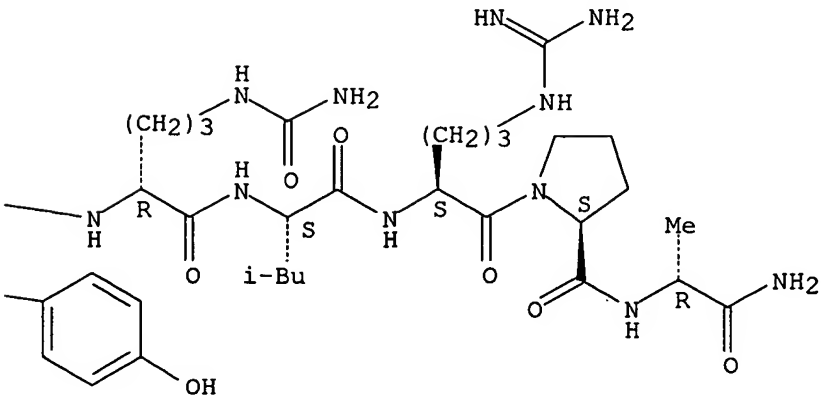


RN 145672-81-7 CAPLUS

CN D-Alaninamide, N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-D-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-L-tyrosyl-N5-(aminocarbonyl)-

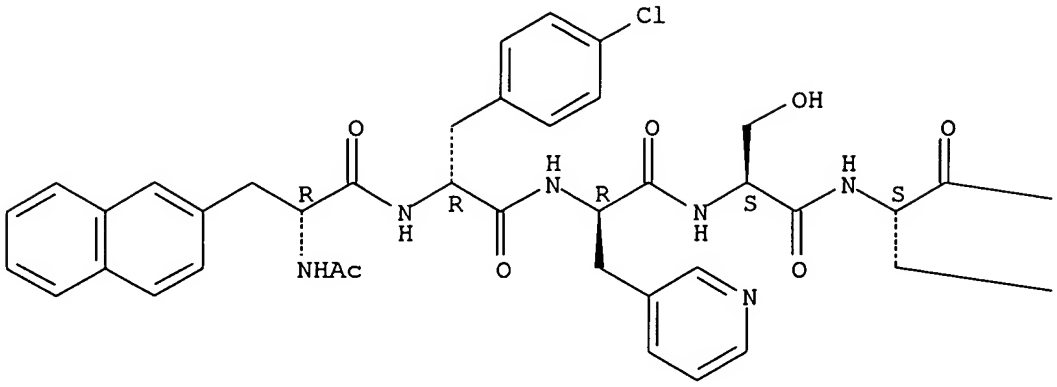
D-ornithyl-L-leucyl-L-arginyl-L-prolyl-, acetate (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 120287-85-6
CMF C70 H92 Cl N17 O14

Absolute stereochemistry.

PAGE 1-A



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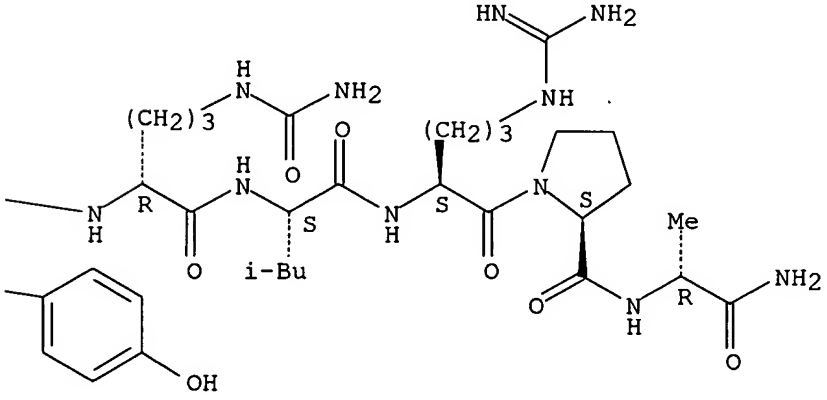
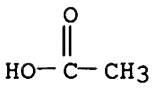


CM 2

CRN 64-19-7
CMF C2 H4 O2



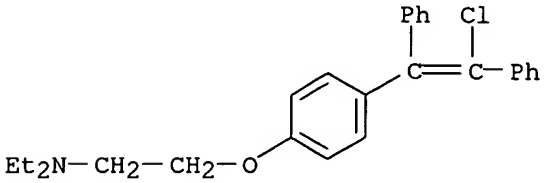
IT 50-41-9, Clomiphene citrate 911-45-5, Clomiphene
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(combination therapy with GnRH antagonist, clomifen citrate, and gonadotropins; LHRH-antagonists in treatment of fertility disorders)

RN 50-41-9 CAPLUS
CN Ethanamine, 2-[4-(2-chloro-1,2-diphenylethenyl)phenoxy]-N,N-diethyl-, 2-hydroxy-1,2,3-propanetricarboxylate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 911-45-5
CMF C26 H28 Cl N O



CM 2

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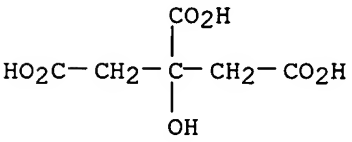

RN 911-45-5 CAPLUS
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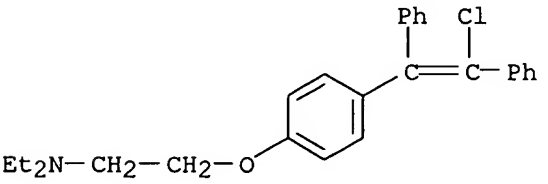

L15 ANSWER 11 OF 55 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER:	2000:39795 CAPLUS
DOCUMENT NUMBER:	132:73850
TITLE:	Will GnRH antagonists provide new hope for patients considered "difficult responders" to GnRH agonist protocols?
AUTHOR(S):	Craft, Ian; Gorgy, Amin; Hill, Jennifer; Menon, David; Podsiadly, Barbara
CORPORATE SOURCE:	London Gynaecology and Fertility Centre, London, W1N 1AF, UK
SOURCE:	Human Reproduction (1999), 14(12), 2959-2962 CODEN: HUREEE; ISSN: 0268-1161
PUBLISHER:	Oxford University Press
DOCUMENT TYPE:	Journal

LANGUAGE: English

AB We have assessed the use of cetrorelix, a gonadotropin releasing hormone (GnRH) antagonist, in conjunction with clomiphene citrate and gonadotropin in 31 in-vitro fertilization (IVF)/gamete intra-Fallopian transfer (GIFT) cycles for 25 difficult responders. Group I included 18 poor responders (24 cycles) with no live birth in 23 previous IVF cycles with GnRH agonists. Group II included seven patients (seven cycles) with polycystic ovaries. Thirteen previous IVF/GIFT cycles with GnRH agonists had resulted in one live birth and three of these patients had developed ovarian hyperstimulation syndrome (OHSS). The treatment protocol involved a daily dose of clomiphene citrate 100 mg for 5 days and gonadotropin injections from cycle day 2. Cetrorelix 0.25 mg/day was started when the leading follicle reached 14 mm. The outcome in both groups was favorable compared to previous treatment with GnRH agonists. In group I the abandoned cycle rate was 29 vs. 57% (P = 0.06). More oocytes were produced (6.4 vs. 4.7 oocytes/cycle) at a lower dose of FSH (FSH) (709 vs. 1163 IU/oocyte; P = 0.08) and two live births resulted (11.8%). In group II fewer oocytes were produced (10.2 vs. 14.5 oocytes/cycle), using a lower dose of gonadotropin (170 vs. 189 IU/oocyte) and resulted in one ongoing pregnancy. No patients experienced OHSS. This report is preliminary and a further controlled randomized study is required.

IT Gonadotropins
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(GnRH antagonists for infertile women considered difficult responders to GnRH agonist protocols)

IT Fertility
(female, disorder; GnRH antagonists for infertile women considered difficult responders to GnRH agonist protocols)

IT Ovary, disease
(hyperstimulation syndrome; GnRH antagonists for infertile women considered difficult responders to GnRH agonist protocols)

IT Fertilization
(in vitro; GnRH antagonists for infertile women considered difficult responders to GnRH agonist protocols)

IT Ovary, disease
(polycystic; GnRH antagonists for infertile women considered difficult responders to GnRH agonist protocols)

IT 50-41-9, Clomiphene citrate 120287-85-6, Cetrorelix
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(GnRH antagonists for infertile women considered difficult responders to GnRH agonist protocols)

IT 9034-40-6, GnRH
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(antagonists; GnRH antagonists for infertile women considered difficult responders to GnRH agonist protocols)

IT 50-41-9, Clomiphene citrate 120287-85-6, Cetrorelix
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(GnRH antagonists for infertile women considered difficult responders to GnRH agonist protocols)

RN 50-41-9 CAPLUS

CN Ethanamine, 2-[4-(2-chloro-1,2-diphenylethenyl)phenoxy]-N,N-diethyl-, 2-hydroxy-1,2,3-propanetricarboxylate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 911-45-5
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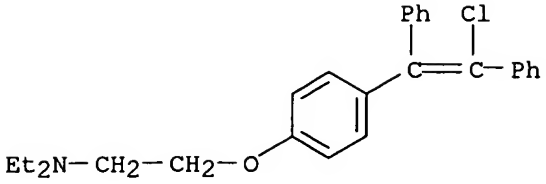

CM 2

CRN 77-92-9
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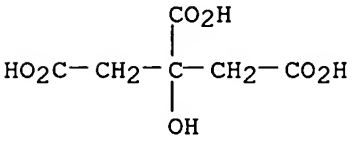
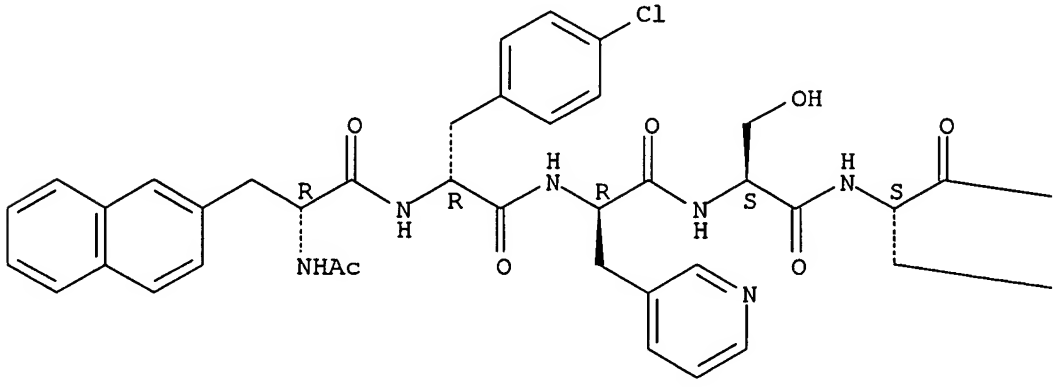
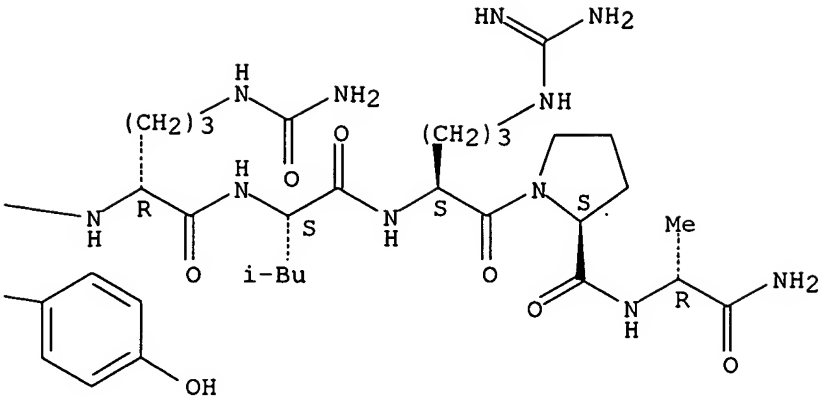


RN 120287-85-6 CAPLUS
CN D-Alaninamide, N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-D-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-L-tyrosyl-N5-(aminocarbonyl)-D-ornithyl-L-leucyl-L-arginyl-L-prolyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.





REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 12 OF 55 USPATFULL on STN
ACCESSION NUMBER: 2006:81036 USPATFULL
TITLE: Use of gnrh agonists to support the luteal phase during infertility treatment
INVENTOR(S): Loumaye, Ernest, Massongy, FRANCE

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2006069031	A1	20060330	
APPLICATION INFO.:	US 2003-540228	A1	20031229	(10)
	WO 2003-IB6205		20031229	
			20050621	PCT 371 date

	NUMBER	DATE
PRIORITY INFORMATION:	FR 2002-16810	20021227
	US 2003-448468P	20030221 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: LAHIVE & COCKFIELD, LLP., 28 STATE STREET, BOSTON, MA, 02109, US
NUMBER OF CLAIMS: 31
EXEMPLARY CLAIM: 1-72
LINE COUNT: 1009
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

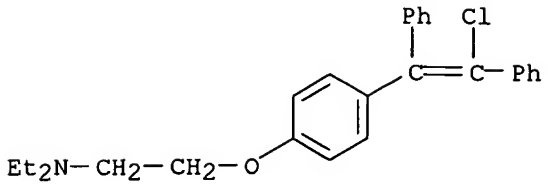
AB The present invention concerns the use of an agonist of an hypothalamic hormone for the preparation of a pharmaceutical agent to support the luteal phase during infertility treatment of female mammals and more specifically of women. According to this invention, the pharmaceutical agent is suitable to be used for supporting the luteal phase after a spontaneous ovulation or after stimulation of follicular growth, trigger of final follicular maturation and ovulation with one or several additional agents.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT Human
IT Ovulation
IT Selective estrogen receptor modulators
(GnRH agonist in the treatment of sterility)
IT Hypothalamic hormones
IT Leukemia inhibitory factor
IT Peptides, biological studies
IT Progestogens

(GnRH agonist in the treatment of sterility)
IT Drug delivery systems
(controlled-release; GnRH agonist in the treatment of sterility)
IT Drug delivery systems
(delayed release; GnRH agonist in the treatment of sterility)
IT Embryo, animal
(embryo implantation-associated cytokines; GnRH agonist in the treatment of sterility)
IT Cytokines
(embryo implantation-associated; GnRH agonist in the treatment of sterility)
IT Sterility
(female; GnRH agonist in the treatment of sterility)
IT Ovary
(follicle; GnRH agonist in the treatment of sterility)
IT Drug delivery systems
(injections, i.m.; GnRH agonist in the treatment of sterility)
IT Drug delivery systems
(injections, s.c.; GnRH agonist in the treatment of sterility)
IT Artificial insemination
(intra-uterine insemination; GnRH agonist in the treatment of sterility)
IT Ovarian cycle
(luteal phase; GnRH agonist in the treatment of sterility)
IT Drug delivery systems
(nasal; GnRH agonist in the treatment of sterility)
IT Egg
(oocyte; GnRH agonist in the treatment of sterility)
IT Drug delivery systems
(oral; GnRH agonist in the treatment of sterility)
IT Drug delivery systems
(pulmonary; GnRH agonist in the treatment of sterility)
IT Drug delivery systems
(rectal; GnRH agonist in the treatment of sterility)
IT Drug delivery systems
(transdermal; GnRH agonist in the treatment of sterility)
IT Drug delivery systems
(vaginal; GnRH agonist in the treatment of sterility)
IT 50-28-2, Estradiol, biological studies
(GnRH agonist in the treatment of sterility)
IT 9034-40-6, GnRH
(GnRH agonist in the treatment of sterility)
IT 50-41-9, Clomiphene citrate 57-83-0, Progesterone, biological studies 58-55-9, Theophylline, biological studies 911-45-5, Clomiphene 9002-61-3, Chorionic gonadotropin 9002-61-3D, Chorionic gonadotropin, analogs 9002-67-9, LH 9002-67-9D, Luteinizing hormone, analogs 9002-68-0, Follicle-stimulating hormone 9002-68-0D, Follicle-stimulating hormone, derivs. 10540-29-1, Tamoxifen 53714-56-0, Leuprorelin 57773-63-4, Triptorelin 57982-77-1, Buserelin 61489-71-2, Menopausal gonadotropin 65807-02-5, Goserelin 76932-56-4, Nafarelin 107868-30-4, Exemestane 112809-51-5, Letrozole 120511-73-1, Anastrozole
(GnRH agonist in the treatment of sterility)
IT 9025-82-5, Phosphodiesterase 9039-48-9, Aromatase
(inhibitors; GnRH agonist in the treatment of sterility)
IT 60-92-4, Cyclic AMP
(modulators; GnRH agonist in the treatment of sterility)
IT 50-41-9, Clomiphene citrate 911-45-5, Clomiphene
(GnRH agonist in the treatment of sterility)
RN 50-41-9 USPATFULL
CN Ethanamine, 2-[4-(2-chloro-1,2-diphenylethenyl)phenoxy]-N,N-diethyl-, 2-hydroxy-1,2,3-propanetricarboxylate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 911-45-5
CMF C26 H28 Cl N O



CM 2

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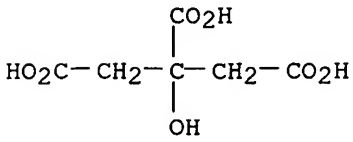
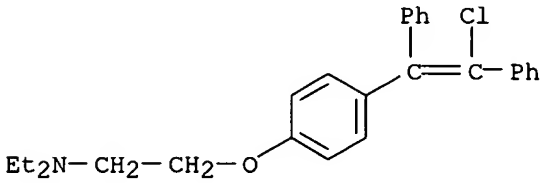


RN 911-45-5 USPATFULL
CN Ethanamine, 2-[4-(2-chloro-1,2-diphenylethenyl)phenoxy]-N,N-diethyl- (9CI) (CA INDEX NAME)



L15 ANSWER 13 OF 55 USPATFULL on STN

ACCESSION NUMBER:	2005:57282 USPATFULL
TITLE:	Use of lh in controlled ovarian hyperstimulation
INVENTOR(S):	Hillier, Stephen G., The Chancellor's Building, 49 Little France Crescent, Edunburgh, UNITED KINGDOM EH16 45B Howles, Colin Michael, Geneva, SWITZERLAND
PATENT ASSIGNEE(S):	Applied Research Systems ARS Holding N. V., Curacao, NETHERLANDS (non-U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2005049199	A1	20050303	
APPLICATION INFO.:	US 2004-487423	A1	20040914	(10)
	WO 2002-GB4147		20020912	

	NUMBER	DATE
PRIORITY INFORMATION:	EP 2001-307755	20010912
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	

LEGAL REPRESENTATIVE: BROWDY AND NEIMARK, P.L.L.C., 624 NINTH STREET, NW, SUITE 300, WASHINGTON, DC, 20001-5303
NUMBER OF CLAIMS: 23
EXEMPLARY CLAIM: 1
LINE COUNT: 808
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention provides a new use for LH, and analogues having LH-activity for aiding folliculogenesis in controlled ovarian hyperstimulation (COH), in which the LH or an analogue thereof is administered during a priming period lasting from day 1 to about day 4 of the stimulatory phase in COH.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT Ovary
(controlled hyperstimulation; methods for the use of LH in controlled ovarian hyperstimulation)
IT Ovary
(follicle; methods for the use of LH in controlled ovarian hyperstimulation)
IT Fertilization
(in vitro; methods for the use of LH in controlled ovarian hyperstimulation)
IT Androgens
IT Estrogens
(levels measurement; methods for the use of LH or hCG in controlled ovarian hyperstimulation and to determine the response of a patient to FSH)
IT Human
(methods for the use of LH in controlled ovarian hyperstimulation)
IT Diagnosis
(methods for the use of LH or hCG in controlled ovarian hyperstimulation and to determine the response of a patient to FSH)
IT 50-28-2, Estradiol, biological studies 63-05-8, Androstenedione
(levels measurement; methods for the use of LH or hCG in controlled ovarian hyperstimulation and to determine the response of a patient to FSH)
IT 9002-67-9, LH 9002-67-9D, LH, analogs and recombinant human (rhLH)
(methods for the use of LH in controlled ovarian hyperstimulation)
IT 9002-61-3, Human chorionic gonadotropin
(methods for the use of LH or hCG in controlled ovarian hyperstimulation)
IT 9002-68-0, FSH
(methods for the use of LH without exogenous FSH in controlled ovarian hyperstimulation)

L15 ANSWER 14 OF 55 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1999:708625 CAPLUS
DOCUMENT NUMBER: 131:295922
TITLE: Method for the treatment of fertility disorders using an LHRH antagonist to partially suppress endogenous gonadotropins during intrauterine insemination
INVENTOR(S): Engel, Jurgen; Riethmuller-Winzen, Hilde; Reissmann, Thomas
PATENT ASSIGNEE(S): Asta Medica Aktiengesellschaft, Germany
SOURCE: PCT Int. Appl., 13 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9955357	A1	19991104	WO 1999-EP2133	19990329

W: AU, BG, BR, BY, CA, CN, CZ, EE, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LT, LV, MK, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TR, UA, UZ, YU, ZA, AM, AZ, MD, TJ, TM
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

CA 2330131	AA	19991104	CA 1999-2330131		19990329
AU 9937028	A1	19991116	AU 1999-37028		19990329
AU 752415	B2	20020919			
BR 9909802	A	20001226	BR 1999-9802		19990329
TR 200003063	T2	20010221	TR 2000-200003063		19990329
EP 1082129	A1	20010314	EP 1999-919152		19990329
EP 1082129	B1	20031029			

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO

JP 2002512975	T2	20020508	JP 2000-545555		19990329
NZ 507405	A	20021025	NZ 1999-507405		19990329
AT 252910	E	20031115	AT 1999-919152		19990329
RU 2221588	C2	20040120	RU 2000-129658		19990329
PT 1082129	T	20040331	PT 1999-919152		19990329
ES 2207941	T3	20040601	ES 1999-919152		19990329
NO 2000005145	A	20001013	NO 2000-5145		20001013
PRIORITY APPLN. INFO.:			US 1998-82743P	P	19980423
			WO 1999-EP2133	W	19990329

AB In the method of therapeutic management of infertility by intrauterine insemination the improvement consisting of (a) the dose-dependent suppression of endogenous gonadotropins, especially LH, with a LH-RH Antagonist allowing the maintenance of physiol. estrogen levels, (b) exogenous stimulation of the ovarian follicle growth, (c) ovulation induction with HCG, native LHRH, LHRH-Agonists or recombinant LH, (d) intrauterine insemination by sperm injection. The LHRH Antagonists may be preferably Cetrorelix or Antarelix. The stimulation is performed by administration of HMG or recombinant FSH with or without recombinant LH or with antiestrogens as for example Chlomiphene as well as with the combination of antiestrogens as for example Chlomiphene with gonadotropins.

IT Estrogens
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antiestrogens; method for treatment of fertility disorders using LHRH antagonist to partially suppress endogenous gonadotropins in combination with ovulation induction and intrauterine insemination)

IT Fertility
(disorder; method for treatment of fertility disorders using LHRH antagonist to partially suppress endogenous gonadotropins during intrauterine insemination)

IT Insemination, artificial
(method for treatment of fertility disorders using LHRH antagonist to partially suppress endogenous gonadotropins during intrauterine insemination)

IT Gonadotropins
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(pituitary; method for treatment of fertility disorders using LHRH antagonist to partially suppress endogenous gonadotropins during intrauterine insemination)

IT 120287-85-6, Cetrorelix 151272-78-5, Antarelix
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(method for treatment of fertility disorders using LHRH antagonist to partially suppress endogenous gonadotropins

during intrauterine insemination)

IT 9034-40-6, LHRH
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(method for treatment of fertility disorders using LHRH antagonist to partially suppress endogenous gonadotropins in combination with ovulation induction and intrauterine insemination)

IT 911-45-5, Clomiphene 9002-61-3, Human chorionic gonadotropin 9002-67-9, LH 9002-68-0, FSH
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(method for treatment of fertility disorders using LHRH antagonist to partially suppress endogenous gonadotropins in combination with ovulation induction and intrauterine insemination)

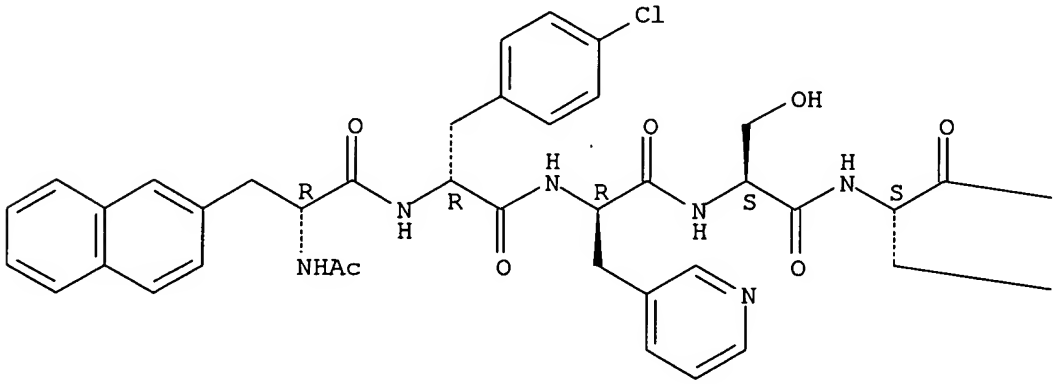
IT 120287-85-6, Cetrorelix
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(method for treatment of fertility disorders using LHRH antagonist to partially suppress endogenous gonadotropins during intrauterine insemination)

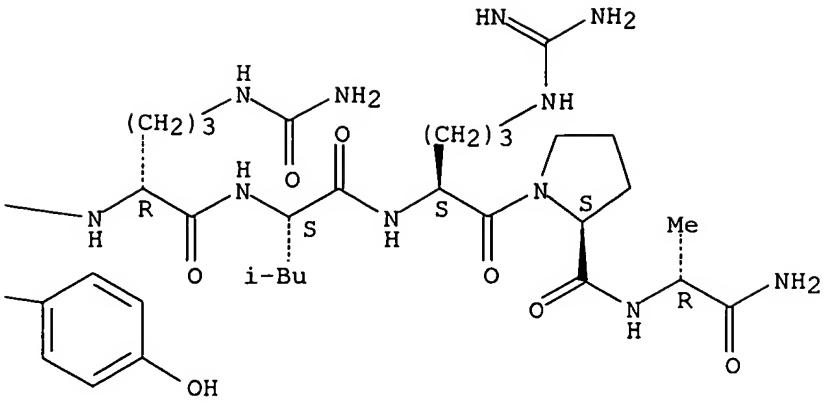
RN 120287-85-6 CAPLUS

CN D-Alaninamide, N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-D-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-L-tyrosyl-N5-(aminocarbonyl)-D-ornithyl-L-leucyl-L-arginyl-L-prolyl- (9CI) (CA INDEX NAME)

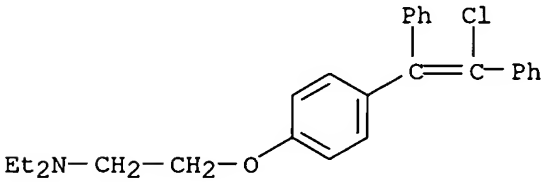
Absolute stereochemistry.

PAGE 1-A





IT 911-45-5, Clomiphene
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(method for treatment of fertility disorders using LHRH antagonist to partially suppress endogenous gonadotropins in combination with ovulation induction and intrauterine insemination)
RN 911-45-5 CAPLUS
CN Ethanamine, 2-[4-(2-chloro-1,2-diphenylethenyl)phenoxy]-N,N-diethyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 15 OF 55 USPATFULL on STN

ACCESSION NUMBER:	2005:270054 USPATFULL			
TITLE:	Method of controlled ovarian hyperstimulation and pharmaceutical kit for use in such method			
INVENTOR(S):	Bunschoten, Evert Johannes, Heesch, NETHERLANDS Coelingh Bennink, Herman Jan Tijmen, Driebergen, NETHERLANDS			

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2005235374	A1	20051020	
APPLICATION INFO.:	US 2003-517028	A1	20030606	(10)
	WO 2003-NL370		20030606	
			20050615	PCT 371 date

	NUMBER	DATE
PRIORITY INFORMATION:	EP 2002-77221	20020607

DOCUMENT TYPE:	Utility
FILE SEGMENT:	APPLICATION
LEGAL REPRESENTATIVE:	Howrey Simon Arnold & White, 321 N Clark Street, Suite 3400, Chicago, IL, 60610, US
NUMBER OF CLAIMS:	20

EXEMPLARY CLAIM: 1
LINE COUNT: 585
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB One aspect of the present invention is concerned with a method of controlled ovarian hyperstimulation in a mammalian female, said method comprising the co-administration to said female of a substance having follicle stimulating hormone activity (FSH substance) in an amount effective to stimulate multiple follicular development;--gonadotropin releasing hormone (GnRH) antagonist in an amount equivalent to a daily subcutaneous dose of at least 0.5 mg ganirelix to prevent a premature LH-surge; and--a LH substance in an amount effective to prevent or suppress symptoms of luteinising hormone (LH) deficiency resulting from the administration of the GnRH antagonist; followed by administering a meiosis and luteinisation inducing substance (ML substance) in an amount effective to stimulate resumption of meiosis and luteinisation, and wherein the LH substance is not obtained from the urine of human females. Another aspect of the to invention relates to a pharmaceutical kit for use in a method of controlled hyperstimulation, which kit comprises:--at least one parenteral or oral dosage unit containing one or more FSH substances in an amount equivalent to a subcutaneous dose of 50-1500 I.U. FSH;--at least one parenteral dosage unit containing one or more GnRH antagonists in an amount equivalent to a subcutaneous dose of 0.5-25 mg ganirelix;--at least one parenteral dosage unit containing one or more LH substances in an amount equivalent to a subcutaneous dose of 50-3000 I.U. recombinant LH; wherein the LH substance is not obtained from the urine of human females.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT Reproduction, animal
(ART (assisted reproductive technol.); method of controlled ovarian hyperstimulation using an FSH substance, LH substance, and a GnRH antagonist and pharmaceutical kit for use in such method)
IT Ovary
(follicle; method of controlled ovarian hyperstimulation using an FSH substance, LH substance, and a GnRH antagonist and pharmaceutical kit for use in such method)
IT Fertilization
(in vitro; method of controlled ovarian hyperstimulation using an FSH substance, LH substance, and a GnRH antagonist and pharmaceutical kit for use in such method)
IT Ovulation
(induction; method of controlled ovarian hyperstimulation using an FSH substance, LH substance, and a GnRH antagonist and pharmaceutical kit for use in such method)
IT Drug delivery systems
IT Human
IT Luteinization
IT Meiosis
(method of controlled ovarian hyperstimulation using an FSH substance, LH substance, and a GnRH antagonist and pharmaceutical kit for use in such method)
IT Egg
(oocyte; method of controlled ovarian hyperstimulation using an FSH substance, LH substance, and a GnRH antagonist and pharmaceutical kit for use in such method)
IT Embryo, animal
(transfer; method of controlled ovarian hyperstimulation using an FSH substance, LH substance, and a GnRH antagonist and pharmaceutical kit for use in such method)
IT 9034-40-6, GnRH
(antagonist; method of controlled ovarian hyperstimulation using an FSH substance, LH substance, and a GnRH antagonist and pharmaceutical kit

for use in such method)

IT 9002-61-3, Chorionic gonadotropin 9002-67-9, Luteinizing hormone 9002-68-0, FSH 120287-85-6, Cetrorelix 120287-85-6D, Cetrorelix, precursor 124904-93-4, Ganirelix 124904-93-4D, Ganirelix, precursor
(method of controlled ovarian hyperstimulation using an FSH substance, LH substance, and a GnRH antagonist and pharmaceutical kit for use in such method)

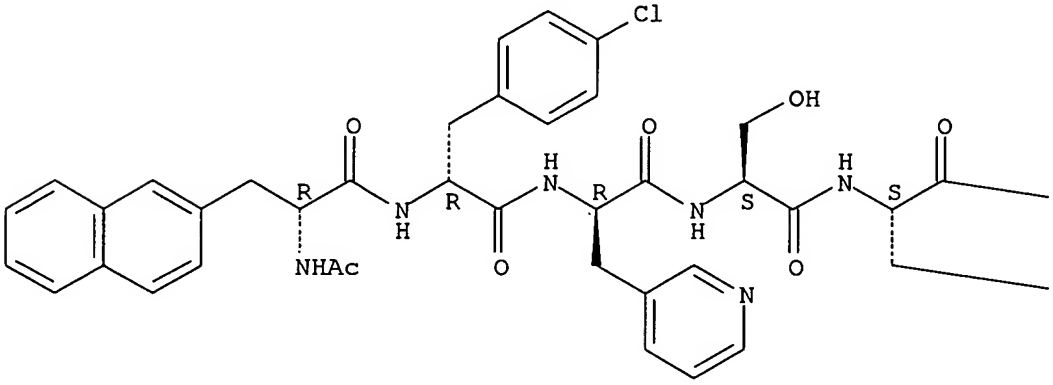
IT 120287-85-6, Cetrorelix 120287-85-6D, Cetrorelix, precursor
(method of controlled ovarian hyperstimulation using an FSH substance, LH substance, and a GnRH antagonist and pharmaceutical kit for use in such method)

RN 120287-85-6 USPATFULL

CN D-Alaninamide, N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-D-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-L-tyrosyl-N5-(aminocarbonyl)-D-ornithyl-L-leucyl-L-arginyl-L-prolyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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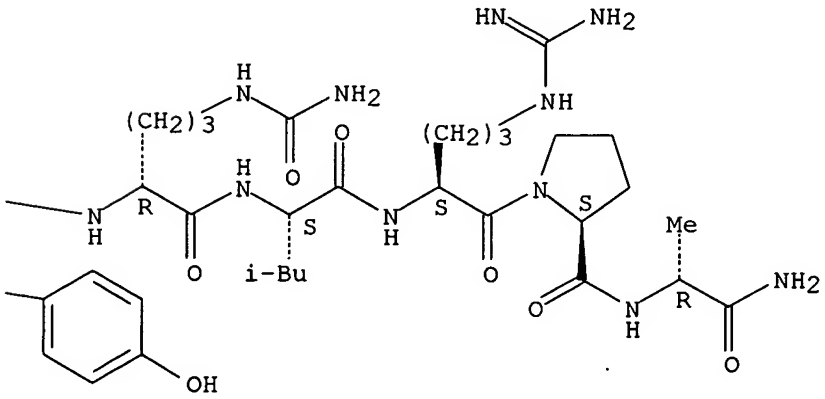
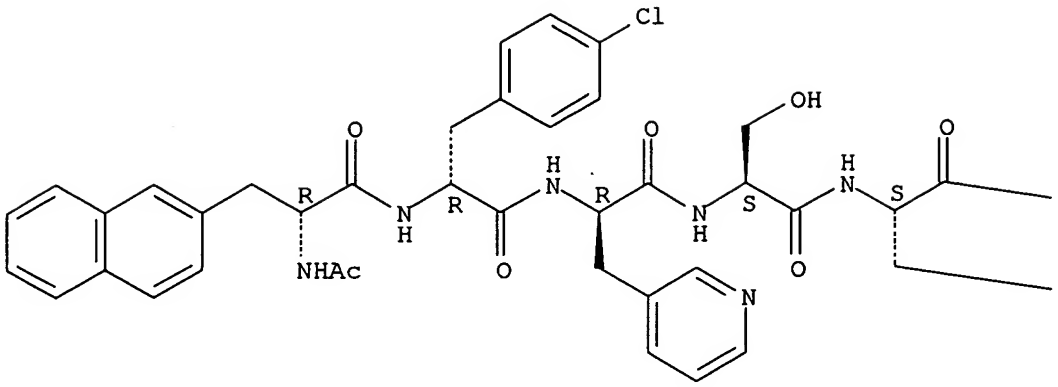


RN 120287-85-6 USPATFULL

CN D-Alaninamide, N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-D-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-L-tyrosyl-N5-(aminocarbonyl)-D-ornithyl-L-leucyl-L-arginyl-L-prolyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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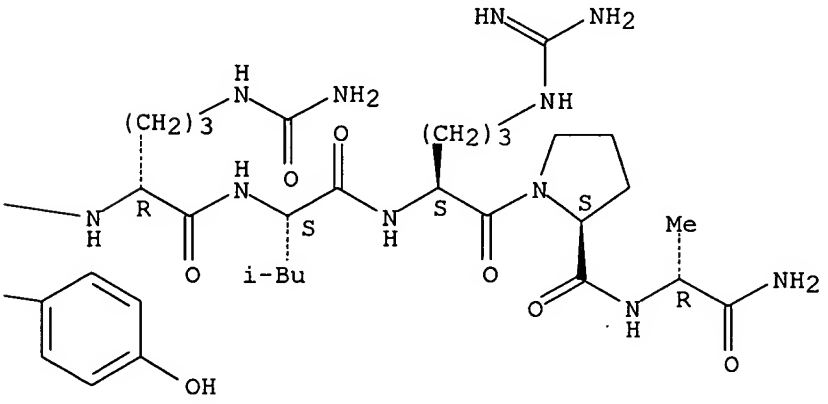


L15 ANSWER 16 OF 55 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2004160066 EMBASE

TITLE: [Comparison of "short protocol" versus "antagosnits" with or without clomiphene citrate for stimulation in IVF of patients with "low response"].
COMPARACION DEL "PROTOCOLO CORTO" VERSUS " ANTAGONISTAS" CON O SIN CITRATO DE CLOMIFENO PARA ESTIMULACIO N EN FIV DE PACIENTES CON "BAJA RESPUESTA".

AUTHOR: Martinez F.; Coroleu B.; Marques L.; Parera N.; Buxaderas R.; Tur R.; Barri P.N.

CORPORATE SOURCE: Dr. F. Martinez, Institut Universitari Dexues, Paseo Bonanova 67, 08017 Barcelona, Spain. Pacmar@dexeus.com

SOURCE: Revista Iberoamericana de Fertilidad y Reproduccion Humana, (2003) Vol. 20, No. 6, pp. 355-360. .
Refs: 18
ISSN: 1132-0249 CODEN: RIFRBG

COUNTRY: Spain

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 003 Endocrinology
010 Obstetrics and Gynecology
021 Developmental Biology and Teratology

030 Pharmacology
037 Drug Literature Index
LANGUAGE: Spanish
SUMMARY LANGUAGE: Spanish; English
ENTRY DATE: Entered STN: 29 Apr 2004
Last Updated on STN: 29 Apr 2004

AB The aim of the study was to evaluate the usefulness of the antagonist Cetrorelix with or without Clomiphene Citrate and urinary or recombinant gonadotropins in the treatment of stimulation for IVF in women with prior low response, compared to the short protocol. Ninety patients were prospectively randomised into four treatment groups: Group A: Short protocol (n= 23). Group B: Cetrorelix + FSHr+HMG (n=21); Group C: Cetrorelix +CC+FSHr; Group D: Cetrorelix+CC+HMG (n=26). All four groups were homogeneous for age, and basal FSH and estradiol. Estradiol levels on day of HCG were significantly lower in group B (938+497 pg/ml), than in the other three groups (A=1579+900pg/ml, C=1044+461 pg/ml, D=1492+901 pg/ml). There were 65 embryo transfer that yielded 18 pregnancies, which gives pregnancy rates of 20% per patient and 27% per embryo transfer There were 7 abortions (38.9%) and 11 ongoing pregnancies. There were not significant differences in pregnancy rates per patient, and per transfer, neither implantation nor abortion rates among four groups. In women with previous low response, antagonists seem to allow a reduction in the total dose of gonadotropins and number of days of treatment, to produce similar pregnancy rates to protocols with agonists.

L15 ANSWER 17 OF 55 EMBASE
ACCESSION NUMBER: 2005521110 EMBASE
TITLE: A pharmacotherapeutic review of treatment options for infertility in women.
AUTHOR: Moultry A.M.; Eaton A.; Che S.
CORPORATE SOURCE: Dr. A.M. Moultry, Department of Pharmacy Practice, College of Pharmacy and Health Sciences, Texas Southern University, Houston, TX, United States
SOURCE: Formulary, (2005) Vol. 40, No. 10, pp. 329-341. .
Refs: 54
ISSN: 1082-801X CODEN: FORMF
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 010 Obstetrics and Gynecology
030 Pharmacology
036 Health Policy, Economics and Management
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 15 Dec 2005
Last Updated on STN: 15 Dec 2005

AB The growing trend for women to wait later in life before having their first child has placed many women at a higher risk for difficult conception. There are numerous classes of medications available to assist women who have been diagnosed with infertility. Agents that are used in the treatment of infertility include: clomiphene citrate, aromatase Inhibitors, gonadotrapins, chorionic gonadotrapins, gonadotropin-releasing hormone, gonadotropin-releasing hormone agonists, gonadotropin-releasing hormone antagonists, follitropins, and other miscellaneous agents. Medications chosen for a patient will vary depending on the identified cause of the infertility. Additionally, economic factors will play a role. It is important for healthcare professionals to be aware of treatment options and have a basic understanding of the role these medications play in the

treatment of infertility.

L15 ANSWER 18 OF 55 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:174479 CAPLUS
DOCUMENT NUMBER: 142:404417
TITLE: Influence of hormonal stimulation on in vitro fertilization/embryo transfer outcome
AUTHOR(S): Bauman, Renato; Vujisic, Sanja; Tripalo, Ana; Aksamija, Alenka; Hafner, Daria; Emedi, Ivana; Kupesic, Sanja
CORPORATE SOURCE: Clinical Laboratory for Human Reproduction, Department of Obstetrics and Gynecology, Medical School, Sveti Duh Hospital, University of Zagreb, Zagreb, 10000, Croatia
SOURCE: European Journal of Obstetrics & Gynecology and Reproductive Biology (2005), 119(1), 94-102
CODEN: EOGRAL; ISSN: 0301-2115
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Objective: To compare efficacy and efficiency of ovarian stimulation therapy. Study design: Retrospective study compares ovarian response as number of retrieved oocytes, fertilization rates, endometrial patterns, number of pregnancies and pregnancy rates to different stimulation protocols. Results: The least number of cancelled cycles was in long protocols with buserelin. There was no difference in overall number of retrieved oocytes between the rFSH and HMG protocols, but 75% of the patients undergoing both protocols had higher number of oocytes after rFSH. The highest pregnancy rate (35.13%) was with rFSH. There was no statistical correlation between endometrial pattern and type of protocol used. Data showed the 9 mm cut-off value for endometrial thickness, and RI = 0.58 for subendometrial blood flow between the pregnant and non-pregnant group of patients. Nitriderm patches significantly decreased subendometrial RI of the patients with impaired uterine perfusion, increased endometrial thickness and achieved better morphol. Conclusions: These findings demonstrate that rFSH alone and in long protocol gives better results in wide patient population. Nitriderm patches seem to have good impact on pregnancy rate, but further studies are necessary before making any statements.
IT Uterus
(endometrium; ovarian hormonal stimulation therapy efficacy and efficiency on in vitro fertilization/embryo transfer outcome and effect on endometrial patterns in women)
IT Fertility
(female; ovarian hormonal stimulation therapy efficacy and efficiency on in vitro fertilization/embryo transfer outcome and effect on endometrial patterns in women)
IT Egg
(oocyte; ovarian hormonal stimulation therapy efficacy and efficiency on in vitro fertilization/embryo transfer outcome and effect on endometrial patterns in women)
IT Circulation
Embryo, animal
Human
In vitro fertilization
Ovulation induction
(ovarian hormonal stimulation therapy efficacy and efficiency on in vitro fertilization/embryo transfer outcome and effect on endometrial patterns in women)
IT 50-41-9, Clomiphene citrate 55-63-0, Transderm-Nitro 57-83-0, Utrogestan, biological studies 9002-61-3, Chorionic gonadotropin 39366-37-5 61489-71-2, Pergonal 65807-02-5, Zoladex 68630-75-1, Buserelin acetate 145672-81-7,

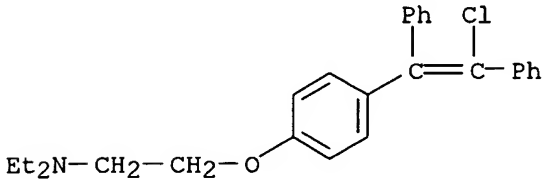
Cetrotide 146479-72-3, Gonal F
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ovarian hormonal stimulation therapy efficacy and efficiency on in vitro fertilization/embryo transfer outcome and effect on endometrial patterns in women)

IT 50-41-9, Clomiphene citrate 145672-81-7, Cetrotide
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ovarian hormonal stimulation therapy efficacy and efficiency on in vitro fertilization/embryo transfer outcome and effect on endometrial patterns in women)

RN 50-41-9 CAPLUS
CN Ethanamine, 2-[4-(2-chloro-1,2-diphenylethenyl)phenoxy]-N,N-diethyl-, 2-hydroxy-1,2,3-propanetricarboxylate (1:1) (9CI) (CA INDEX NAME)

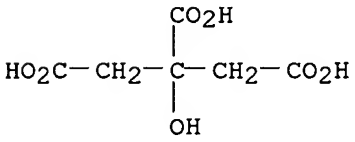
CM 1

CRN 911-45-5
CMF C26 H28 Cl N O



CM 2

CRN 77-92-9
CMF C6 H8 O7



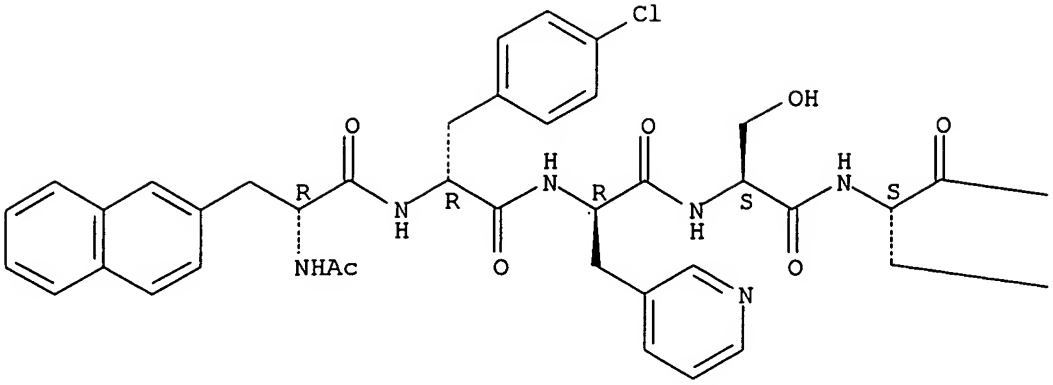
RN 145672-81-7 CAPLUS
CN D-Alaninamide, N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-D-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-L-tyrosyl-N5-(aminocarbonyl)-D-ornithyl-L-leucyl-L-arginyl-L-prolyl-, acetate (salt) (9CI) (CA INDEX NAME)

CM 1

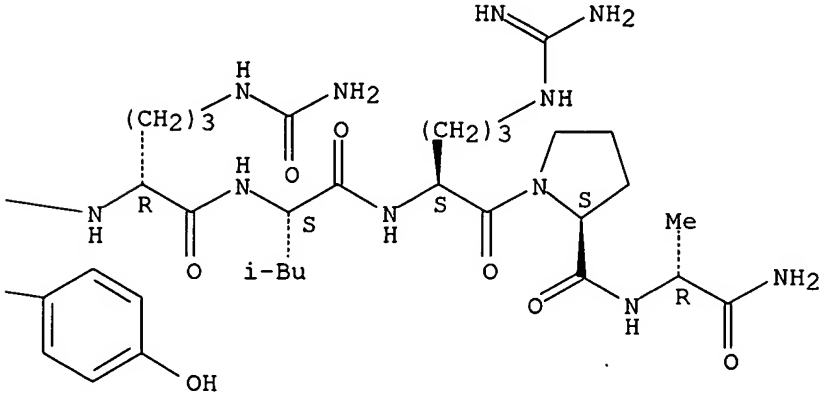
CRN 120287-85-6
CMF C70 H92 Cl N17 O14

Absolute stereochemistry.

PAGE 1-A

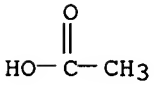


PAGE 1-B



CM 2

CRN 64-19-7
CMF C2 H4 O2



REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 19 OF 55 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:725497 CAPLUS
DOCUMENT NUMBER: 133:261948
TITLE: Method for a programmed controlled ovarian stimulation protocol
INVENTOR(S): Engel, Jurgen; Riethmuller-winzen, Hilde
PATENT ASSIGNEE(S): Asta Medica A.-G., Germany
SOURCE: PCT Int. Appl., 17 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2000059542	A1	20001012	WO 2000-EP2466		20000321
W: AU, BG, BR, BY, CA, CN, CZ, EE, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LT, LV, MK, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TR, UA, UZ, YU, ZA, AM, AZ, MD, TJ, TM					
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE					
CA 2367214	AA	20001012	CA 2000-2367214		20000321
AU 2000041069	A5	20001023	AU 2000-41069		20000321
AU 768544	B2	20031218			
EP 1165138	A1	20020102	EP 2000-920521		20000321
EP 1165138	B1	20040506			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO					
BR 2000009477	A	20020108	BR 2000-9477		20000321
JP 2002541122	T2	20021203	JP 2000-609104		20000321
NZ 514964	A	20030829	NZ 2000-514964		20000321
RU 2226395	C2	20040410	RU 2001-129500		20000321
AT 265862	E	20040515	AT 2000-920521		20000321
PT 1165138	T	20040930	PT 2000-920521		20000321
ES 2219331	T3	20041201	ES 2000-920521		20000321
NO 2001004736	A	20011126	NO 2001-4736		20010928
ZA 2001007974	A	20020806	ZA 2001-7974		20010928
BG 106045	A	20020531	BG 2001-106045		20011024
PRIORITY APPLN. INFO.:			US 1999-127241P	P	19990331
			US 1999-131632P	P	19990428
			WO 2000-EP2466	W	20000321

AB A method of therapeutic management of infertility by programming of controlled ovarian stimulation (COS) and assisted reproductive procedures (ART) the improvement consisting of (a) suppression of premature ovulation with an LHRH-antagonist in controlled ovarian stimulation (COS) and assisted reproductive techniques (ART) with multiple follicle and oocyte development; (b) programming the start of controlled ovarian stimulation (COS) by the administration of progestogen only - or alternatively combined oral contraceptive prepns.; (c) exogenous stimulation of the ovarian follicle growth; (d) ovulation induction with HCG, native LHRH, LHRH-agonists or recombinant LH; (e) application of assisted reproduction techniques, especially of IVF, ICSI, GIFT, ZIFT or by intrauterine insemination by sperm injection.

IT Gamete and Germ cell
(GIFT (gamete intra-fallopian transfer); method for a programmed controlled ovarian stimulation protocol using LHRH antagonists for the prevention of premature ovulation)

IT Sperm
(ICSI (intracytoplasmic sperm injection) and intrauterine insemination by sperm injection; method for a programmed controlled ovarian stimulation protocol using LHRH antagonists for the prevention of premature ovulation)

IT Estrogens
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antiestrogens, controlled ovarian stimulation by; method for a programmed controlled ovarian stimulation protocol using LHRH antagonists for the prevention of premature ovulation)

IT Gonadotropins
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(controlled ovarian stimulation by combination of antiestrogens and gonadotropins; method for a programmed controlled ovarian stimulation protocol using LHRH antagonists for the prevention of premature ovulation)

IT Fertility
(disorder; method for a programmed controlled ovarian stimulation protocol using LHRH antagonists for the prevention of premature ovulation)

IT Ovary
(follicle; method for a programmed controlled ovarian stimulation protocol using LHRH antagonists for the prevention of premature ovulation)

IT Fertilization
(in vitro; method for a programmed controlled ovarian stimulation protocol using LHRH antagonists for the prevention of premature ovulation)

IT Ovary
Ovulation
(method for a programmed controlled ovarian stimulation protocol using LHRH antagonists for the prevention of premature ovulation)

IT Contraceptives
(oral, ovarian stimulation with progestogens or oral contraceptives; method for a programmed controlled ovarian stimulation protocol using LHRH antagonists for the prevention of premature ovulation)

IT Progestogens
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ovarian stimulation with progestogens or oral contraceptives; method for a programmed controlled ovarian stimulation protocol using LHRH antagonists for the prevention of premature ovulation)

IT Embryo, animal
(zygote, ZIFT (zygote intra-fallopian transfer); method for a programmed controlled ovarian stimulation protocol using LHRH antagonists for the prevention of premature ovulation)

IT 911-45-5, Clomiphene 9002-68-0, FSH
61489-71-2, Human menopausal gonadotropin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(controlled ovarian stimulation by; method for a programmed controlled ovarian stimulation protocol using LHRH antagonists for the prevention of premature ovulation)

IT 9002-67-9, LH
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(for ovulation induction; method for a programmed controlled ovarian stimulation protocol using LHRH antagonists for the prevention of premature ovulation)

IT 9034-40-6, LHRH 112568-12-4, Antide 120287-85-6, Cetrorelix 124904-93-4, Ganirelix 144743-92-0, Teverelix 183552-38-7, Abarelix
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(method for a programmed controlled ovarian stimulation protocol using LHRH antagonists for the prevention of premature ovulation)

IT 57-63-6D, Ethinylestradiol, progestogen mixture 72-33-3D, Mestranol, progestogen mixture
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

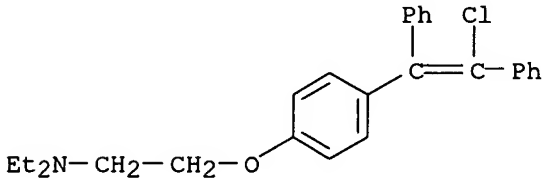
(ovarian stimulation with progestogens or oral contraceptives; method for a programmed controlled ovarian stimulation protocol using LHRH antagonists for the prevention of premature ovulation)

IT 9002-61-3, Human chorionic gonadotropin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ovulation induction by; method for a programmed controlled ovarian stimulation protocol using LHRH antagonists for the prevention of premature ovulation)

IT 911-45-5, Clomiphene
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(controlled ovarian stimulation by; method for a programmed controlled ovarian stimulation protocol using LHRH antagonists for the prevention of premature ovulation)

RN 911-45-5 CAPLUS

CN Ethanamine, 2-[4-(2-chloro-1,2-diphenylethenyl)phenoxy]-N,N-diethyl- (9CI) (CA INDEX NAME)



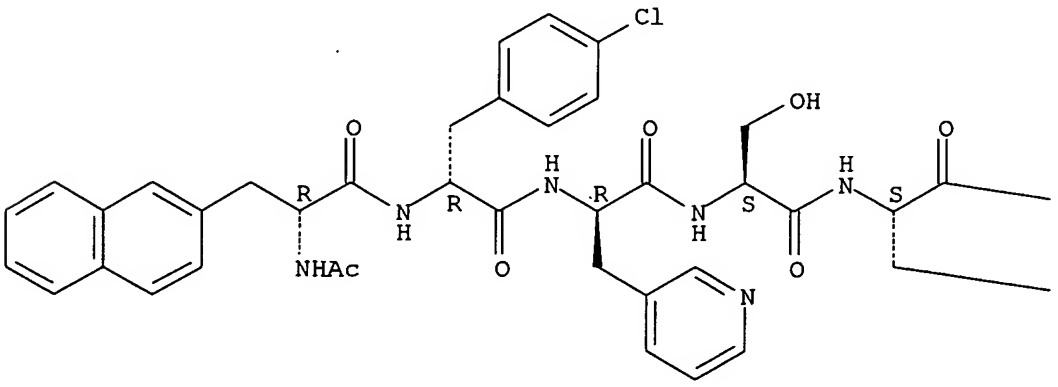
IT 120287-85-6, Cetrorelix
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(method for a programmed controlled ovarian stimulation protocol using LHRH antagonists for the prevention of premature ovulation)

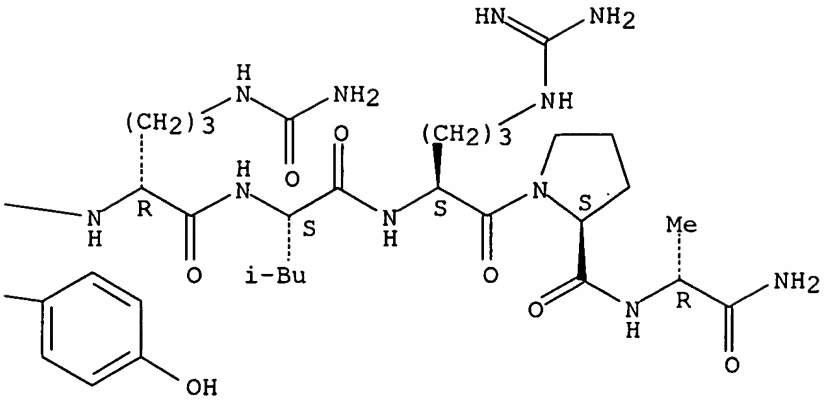
RN 120287-85-6 CAPLUS

CN D-Alaninamide, N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-D-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-L-tyrosyl-N5-(aminocarbonyl)-D-ornithyl-L-leucyl-L-arginyl-L-prolyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A





REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 20 OF 55 MEDLINE on STN
ACCESSION NUMBER: 2003103859 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12580839
TITLE: The use of clomiphene citrate/human menopausal gonadotrophins in conjunction with GnRH antagonist in an IVF/ICSI program is not a cost effective protocol.
AUTHOR: Mansour Ragga; Aboulghar Mohammed; Serour Gamal I; Al-Inany Hesham G; Fahmy Ibrahim; Amin Yehia
CORPORATE SOURCE: The Egyptian IVF-ET Center, Maadi, Egypt.. ivf@link.net
SOURCE: Acta obstetricia et gynecologica Scandinavica, (2003 Jan) Vol. 82, No. 1, pp. 48-52.
Journal code: 0370343. ISSN: 0001-6349.
PUB. COUNTRY: Denmark
DOCUMENT TYPE: (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200303
ENTRY DATE: Entered STN: 6 Mar 2003
Last Updated on STN: 22 Mar 2003
Entered Medline: 21 Mar 2003

AB OBJECTIVE: To evaluate the cost effectiveness of a clomiphene citrate (CC)/human menopausal gonadotropin (hMG)/GnRH antagonist protocol versus a long-acting GnRH agonist/hMG protocol. PARTICIPANTS AND METHODS: One hundred eighty nine couples having their first trial of ICSI for male factor infertility were divided into two groups. Group I (no = 33) received CC 100-150 mg/day for five days starting from day 2 of the cycle and 150 IU of hMG/day on days 6-10. GnRH antagonist (Centrorelix) 0.25 mg/day was started when the leading follicle reached 16 mm in the absence of an LH surge. Group II (no = 156) received 0.1 mg Deacapeptyl/day as our standard long protocol. RESULTS: Clinical pregnancy was observed in 8 out of the 33 cases in group I (24%) while in group II, 92 out of 156 achieved clinical pregnancy (59%), the difference was statistically significant (P = 0.019). The cost of medications/cycle was estimated to be 1110+/-492 E.P in group I, while it was 1928+/-456 E.P. in group II. However, the total cost per pregnancy was 19653 EP in group I and 10047 EP in group II. CONCLUSION: The use of the clomid/hMG/antagonist protocol is not a cost effective strategy and should not be recommended in IVF-ICSI cycles.

L15 ANSWER 21 OF 55 USPATFULL on STN
ACCESSION NUMBER: 2001:208180 USPATFULL

TITLE: Method for the treatment of fertility disorders

INVENTOR(S): Engel, Jurgen, Alzenau, Germany, Federal Republic of
Riethmuller-Winzen, Hilde, Frankfurt, Germany, Federal Republic of
Reissmann, Thomas, Frankfurt, Germany, Federal Republic of

PATENT ASSIGNEE(S): Zentaris AG, Frankfurt am Main, Germany, Federal Republic of (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6319192	B1	20011120
APPLICATION INFO.:	US 1999-296610		19990423 (9)

	NUMBER	DATE
PRIORITY INFORMATION:	US 1998-82743P	19980423 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Lacyk, John P.
ASSISTANT EXAMINER: Cadugan, Joseph A
LEGAL REPRESENTATIVE: Pillsbury Winthrop LLP
NUMBER OF CLAIMS: 6
EXEMPLARY CLAIM: 1
LINE COUNT: 123

AB An improvement to the method of intrauterine insemination by the administration of luteinizing hormone-releasing hormone antagonists (LHRH antagonists).

L15 ANSWER 22 OF 55 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2003404323 EMBASE
TITLE: Drugs used in reproductive medicine.
AUTHOR: Lavery S.
CORPORATE SOURCE: S. Lavery, Department of Reproductive Medicine, Hammersmith Hospital, Du Cane Road, London W12 0HS, United Kingdom. stuart.lavery@imperial.ac.uk
SOURCE: Current Obstetrics and Gynaecology, (2003) Vol. 13, No. 6, pp. 355-361. .
Refs: 4
ISSN: 0957-5847 CODEN: COGYFP
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 010 Obstetrics and Gynecology
027 Biophysics, Bioengineering and Medical Instrumentation
037 Drug Literature Index
038 Adverse Reactions Titles
039 Pharmacy
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 23 Oct 2003
Last Updated on STN: 23 Oct 2003

AB This article discusses some important and commonly used drugs in reprove medicine, concentrating on the management of subfertility. Clomiphene citrate effective first-line therapy in anovulation, resulting in 80% ovulation rates and 50-60% pregnancy rates. Gonadotrophins are effective ovulation- induction agents in cases of clomiphene resistance or for super ovulation protocols necessary for in-vitro fertilization. The debate about recombinant vs highly purified urinary gonadotrophins continues. Metformin and aromatase

inhibitors show promise but further evidence is needed to support their routine use. Both gonadotrophin-releasing homone agonists and antagonists are effective at preventing a premature surge of luteinizing hormone, but ir it is unclear whether the antagonists, with their patient-friendly shorter cycle, will become the approach of choice. Concerns about the carcinogenic effects of infertility drugs do not seem to be supported by epidemiological evidence, but because of a possible time-lag effect, this area merits surveillance. Future developments include more patient-friendly drug-delivery systems. .COPYRGT. 2003 Published by Elsevier Ltd.

L15 ANSWER 23 OF 55 MEDLINE on STN
ACCESSION NUMBER: 2003544280 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14623556
TITLE: [Revisiting the clomifene-gonadotropin protocol in IVF with the use of a GnRH antagonist]. Rehabilitation du protocole clomiphene -gonadotrophines en FIV par l'utilisation d'un antagoniste du GnRH.
AUTHOR: Emperaire J-C; Parneix I; Perraguin-Jayot S
CORPORATE SOURCE: Centre de FIV Aquitaine-Sante, clinique Jean-Villar, 33520 Bruges, France.. jc.emperaire@aquitanesante.fr
SOURCE: Gynecologie, obstetrique & fertilite, (2003 Nov) Vol. 31, No. 11, pp. 927-31.
Journal code: 100936305. ISSN: 1297-9589.
PUB. COUNTRY: France
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: French
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200402
ENTRY DATE: Entered STN: 19 Nov 2003
Last Updated on STN: 11 Feb 2004
Entered Medline: 10 Feb 2004
AB OBJECTIVE: To assess the ability of GnRH antagonists to prevent LH surges during superovulation for IVF in classical stimulation protocols with clomiphene and gonadotropins. PATIENTS AND METHODS: Fifty-eight patients were treated with clomiphene (100 mg daily for 5 days starting on cycle day 2) and gonadotropins (225 UI HMG on cycle days 5, 7 and 9), with monitoring starting on cycle day 10. Cetrorelix, 0.25 mg, was administered daily when dominant follicle diameter reached 18 mm and/or plasma estradiol levels 800 pg/ml. RESULTS: No premature LH surge was observed during the 48 stimulation cycles completed. The pregnancy rate was 20.8% per punction and 25.6% per transfer, and there was no clinical ovarian hyperstimulation syndrome in these series. CONCLUSIONS: Cetrorelix, 0.25 mg, optimizes the classical stimulation with clomiphene and gonadotropins by preventing LH surges; the so-completed protocol yields acceptable pregnancy rates with lower hormone quantities and reduced risks of ovarian hyperstimulation, and becomes a convenient choice when "softer" treatments for IVF are considered.

L15 ANSWER 24 OF 55 EMBASE
ACCESSION NUMBER: 2001393055 EMBASE
TITLE: [How to treat anovulation in case of infertility ?].
COMMENTTRAITER L'ANOVULATION EN CAS D'INFERTILITE?.
AUTHOR: Antoine J.-M.; Merviel P.; Uzan S.
CORPORATE SOURCE: J.-M. Antoine, Serv. de Gynecologie-Obstetrique, Hopital Tenon, 4, rue de la Chine, 75020 Paris, France
SOURCE: Reproduction Humaine et Hormones, (2001) Vol. 14, No. 3, pp. 133-138. .

Refs: 42
ISSN: 0994-3919 CODEN: RHHOED
COUNTRY: France
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 003 Endocrinology
010 Obstetrics and Gynecology
037 Drug Literature Index
LANGUAGE: French
SUMMARY LANGUAGE: English; French
ENTRY DATE: Entered STN: 26 Nov 2001
Last Updated on STN: 26 Nov 2001

AB In PCO patients without male or tubal infertility factors, clomiphene citrate remains the first option for ovarian stimulation. In case of failure, exogenous gonadotrophins (hMG; u-FSH or rec-FSH). are given preferably in step-up low-dose, step-down or combined protocol. Several associated treatements can reduce endogenous gonadotrophins, hyperinsulinism and/or plasma androgens. The surgical approach is suitable for clomiphene citrate resistant PCO with difficult ovarian stimulation or previous OHSS. IVF is recommanded in case of stimulation failure, especially habitual multifollicular development with several cancelled cycles, or in case of associated tubal and/or male factors.

ACCESSION NUMBER: 2003228219 EMBASE
TITLE: Gonadotropin-releasing hormone antagonists: Impact of IVF practice and potential non-assisted reproductive technology applications.
AUTHOR: Tarlatzis B.C.; Bili H.N.
CORPORATE SOURCE: Dr. B.C. Tarlatzis, Infertility and IVF Center, Geniki Kliniki, 2 Gravias Street, Thessaloniki 546 45, Greece. tarlatzis@hol.gr
SOURCE: Current Opinion in Obstetrics and Gynecology, (2003) Vol. 15, No. 3, pp. 259-264. .
Refs: 58
ISSN: 1040-872X CODEN: COOGEA
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 010 Obstetrics and Gynecology
030 Pharmacology
036 Health Policy, Economics and Management
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 19 Jun 2003
Last Updated on STN: 19 Jun 2003

AB Purpose of review: To provide the clinician with updated knowledge of the most recent findings on the clinical use of gonadotropin -releasing hormone antagonists. Recent findings: Gonadotropin -releasing hormone antagonists, which have recently been introduced in clinical practice, cause an immediate suppression of gonadotropin secretion by competitive blocking of pituitary gonadotropin -releasing hormone receptors. Thus, they are effective in preventing the premature luteinizing hormone surges during ovarian stimulation for in-vitro fertilization and may improve the patient's response to lower doses of gonadotropins. Better patient acceptance, shorter treatment cycles and fewer follicles and oocytes are also reported. Data existing so far concerning the necessity of luteal phase support after the use of gonadotropin-releasing hormone antagonists show that it might not be mandatory when used in clomiphene citrate costimulated cycles or in intrauterine insemination cycles. The use of

gonadotropin-releasing hormone antagonists seems to be safe for pregnant women and their offspring. All sex-hormone-dependent disorders, currently treated with gonadotropin-releasing hormone agonists, may in future be indications for a gonadotropin-releasing hormone antagonist, including endometriosis, leiomyoma, and breast cancer in women, benign prostatic hypertrophy and prostatic carcinoma in men, and central precocious puberty in children. The vast majority of the available clinical data up till now, however, are in assisted reproduction and prostate cancer. Summary: It is expected that the availability of gonadotropin-releasing hormone antagonist will lead to the use of 'softer' ovarian stimulation protocols, which will be shorter, cheaper and safer compared with the conventional protocols. .COPYRGT. 2003 Lippincott Williams & Wilkins.

L15 ANSWER 26 OF 55 MEDLINE on STN

ACCESSION NUMBER: 2002204672 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11937125
TITLE: Effect of clomiphene citrate on follicular and luteal phase luteinizing hormone concentrations in in vitro fertilization cycles stimulated with gonadotropins and gonadotropin-releasing hormone antagonist.
AUTHOR: Tavaniotou Asimina; Albano Carola; Smitz Johan; Devroey Paul
CORPORATE SOURCE: Centre for Reproductive Medicine, Dutch-Speaking Free University of Brussels, Brussels, Belgium.. mtavaniotou@hotmail.com
SOURCE: Fertility and sterility, (2002 Apr) Vol. 77, No. 4, pp. 733-7.
Journal code: 0372772. ISSN: 0015-0282.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200301
ENTRY DATE: Entered STN: 9 Apr 2002
Last Updated on STN: 31 Jan 2003
Entered Medline: 30 Jan 2003

AB OBJECTIVE: To investigate the effect that clomiphene citrate exerts on luteinizing hormone (LH) concentrations in gonadotropin /gonadotropin-releasing hormone (GnRH) antagonist cycles. DESIGN: Retrospective analysis. SETTING: Tertiary referral center. PATIENT(S): Two groups of patients undergoing in vitro fertilization (IVF) were compared. In group I, 20 patients were stimulated with clomiphene citrate (CC) in combination with gonadotropins and 0.25 mg of Cetrorelix (ASTA Medica AG; Frankfurt am Main, Germany) and in group II, 20 patients were stimulated with gonadotropins and 0.25 mg of Cetrorelix. INTERVENTION(S): Blood sampling was performed in the late follicular, periovulatory, early, mid, and late luteal phases. MAIN OUTCOME MEASURE(S): Luteinizing hormone (LH), estradiol, and progesterone. RESULT(S): LH levels were significantly higher in group I than in group II on all the days studied. Progesterone serum concentrations were significantly higher in group II in the early luteal phase, but not in the follicular or the middle and late luteal phases. CONCLUSION(S): LH concentrations are significantly higher in the follicular and luteal phases in cycles stimulated with CC, despite GnRH antagonist administration. This observation might have implications for the dose of GnRH antagonist needed to suppress LH in the follicular phase and questions the need for luteal-phase supplementation in cycles in which CC was used.

L15 ANSWER 27 OF 55 EMBASE

ACCESSION NUMBER: 2005226352 EMBASE
TITLE: Emerging drugs in assisted reproduction.
AUTHOR: Papanikolaou E.G.; Kolibianakis E.; Devroey P.
CORPORATE SOURCE: Dr. E.G. Papanikolaou, AZ-VUB, University Hospital, Dutch-Speaking Brussels Free University, Laarbeeklaan 101, 1090 Jette, Brussels, Belgium. Evangelos.Papanikolaou@vub.ac.be
SOURCE: Expert Opinion on Emerging Drugs, (2005) Vol. 10, No. 2, pp. 425-440. .
Refs: 84
ISSN: 1472-8214 CODEN: EOEDA3
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 010 Obstetrics and Gynecology
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 9 Jun 2005
Last Updated on STN: 9 Jun 2005

AB Infertility affects .apprx. 15% of couples of reproductive age. In assisted reproductive technology (ART), medications play a crucial role in stimulating ovaries to produce several oocytes and prepare the endometrium to be receptive after replacing one or more embryos into the uterine cavity. The availability of recombinant human follicle stimulating hormone, luteinising hormone and human chorionic gonadotrophin; of gonadotrophin-releasing hormone (GnRH) agonists and antagonists; and of luteal supplementation with progesterone have allowed the tailoring of several stimulation schemes, which have enhanced the pregnancy outcome after ART treatment. However, the remaining risk of ovarian hyperstimulation syndrome, the still low implantation rates, the unacceptably high rates of multiple pregnancies and the daily parenteral administration of medications do not constitute the features of a patient-friendly procedure. Therefore, a number of molecules with gonadotrophin-like activity, inhibition of GnRH receptor ability, or endometrium receptivity enhancement properties are currently under active investigation. Orally bioactive therapeutic preparations, in particular, may revolutionise in vitro fertilisation (IVF) treatment in the near future. Nevertheless, the implementation of mild ovarian stimulation protocols with single embryo transfer policy and further development of oocyte in vitro maturation techniques may lead to a less drug orientated IVF treatment. .COPYRGT. 2005 Ashley Publications Ltd.

ACCESSION NUMBER: 2006172248 EMBASE
TITLE: Persistent megalocystic ovary following in vitro fertilization in a postpartum patient with polycystic ovarian syndrome.
AUTHOR: Ling S.-Y.; Chong K.-M.; Hwang J.-L.
CORPORATE SOURCE: Dr. J.-L. Hwang, Department of Obstetrics, Shin-Kong Wu Ho Su Memorial Hospital, 95 Wen Chang Road, Shih-Lin District, Taipei, Taiwan,Province of China. b8401161@tmu.edu.tw
SOURCE: Taiwanese Journal of Obstetrics and Gynecology, (2006) Vol. 45, No. 1, pp. 70-72. .
Refs: 14
ISSN: 1028-4559
COUNTRY: Hong Kong
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 010 Obstetrics and Gynecology
037 Drug Literature Index
LANGUAGE: English

SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 3 May 2006
Last Updated on STN: 3 May 2006

AB Objective: Ovarian hyperstimulation syndrome (OHSS) Is more severe when pregnancy occurs, as the developing pregnancy produces human chorionic gonadotropin, which stimulates the ovary's persistent growth. If no pregnancy occurs, the syndrome will typically resolve within 1 week. In a maintained pregnancy, slow resolution of symptoms usually occurs over 1-2 months. Case Report: A 31-year-old woman, gravida 2, para 1, aborta 1, with polycystic ovary syndrome underwent in vitro fertilization (IVF) with clomiphene citrate and follicle-stimulating hormone/gonadotropin releasing hormone-antagonist stimulation. During transvaginal oocyte retrieval, enlarged bilateral ovaries were noted. She had an episode of OHSS after IVF/embryo transfer, for which paracentesis was performed three times. Pregnancy was achieved. Throughout antenatal examinations, bilateral ovaries were enlarged. She delivered a healthy baby by cesarean section at term. However, 1 month after delivery, the bilateral ovary had not shrunk, and levels of tumor markers CA125 and CA199 were 50.84 and 41.34 U/mL, respectively. At laparotomy for suspected malignancy, both adnexae formed "kissing ovaries", which were multinodulated with yellow serous fluid. Specimens from wedge resection submitted for frozen section showed a benign ovarian cyst. The final pathology report showed bilateral follicle cysts. Conclusion: With the increasing use of gonadotropins in the management of infertility, ovarian enlargement secondary to hyperstimulation is common. Generally, symptoms appear between the 6(th) and 13 (th) weeks of pregnancy and disappear thereafter. The hyperstimulated ovary often subsides after the first trimester. This case is unusual as the megalocystic ovary persisted after delivery. To the best of our knowledge, we report the first case of enlarged bilateral ovaries persisting 2 months after delivery.

L15 ANSWER 29 OF 55 USPATFULL on STN
ACCESSION NUMBER: 2004:334208 USPATFULL
TITLE: Normalization of defective T cell responsiveness through manipulation of thymic regeneration
INVENTOR(S): Boyd, Richard L., Hampton, AUSTRALIA
PATENT ASSIGNEE(S): Monash University (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2004265285	A1	20041230
APPLICATION INFO.:	US 2003-749118	A1	20031230 (10)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 2003-419066, filed on 18 Apr 2003, PENDING Continuation-in-part of Ser. No. US 2001-976599, filed on 12 Oct 2001, PENDING Continuation-in-part of Ser. No. US 2001-966575, filed on 26 Sep 2001, ABANDONED Continuation-in-part of Ser. No. US 2001-755983, filed on 5 Jan 2001, ABANDONED Continuation-in-part of Ser. No. US 2000-795286, filed on 13 Oct 2000, ABANDONED Continuation-in-part of Ser. No. US 2000-795302, filed on 13 Oct 2000, ABANDONED

	NUMBER	DATE
PRIORITY INFORMATION:	AU 1999-9778	19990415
	AU 2000-745	20001013
	WO 2000-AU329	20000417
	WO 2002-AU101291	20020418
	US 2003-527001P	20031205 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: WILMER CUTLER PICKERING HALE AND DORR LLP, 60 STATE

STREET, BOSTON, MA, 02109
NUMBER OF CLAIMS: 72
EXEMPLARY CLAIM: CLM-01-28
NUMBER OF DRAWINGS: 53 Drawing Page(s)
LINE COUNT: 4212
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present disclosure provides methods for the treatment and potential alleviation of autoimmune diseases and allergies in a patient. This is accomplished by deleting at least most of the existing T cell population and reactivating the thymus. Optionally, hematopoietic stem cells, autologous, syngeneic, allogeneic or xenogeneic, are delivered to increase the speed of regeneration of the patient's immune system and to supply normal T cells to the patient or to replace existing aberrant T cells. In some embodiments, the hematopoietic stem cells are CD34+. The patient's thymus is reactivated by disruption of sex steroid mediated signaling to the thymus. In some embodiments, this disruption is created by administration of LHRH agonists, LHRH antagonists, anti-LHRH receptor antibodies, anti-LHRH vaccines or combinations thereof.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT CD antigens
(CD11C; normalization of defective T cell responsiveness through manipulation of thymic regeneration, and use in treatment of autoimmune disease and allergy)

IT T cell (lymphocyte)
(NKT cell; normalization of defective T cell responsiveness through manipulation of thymic regeneration, and use in treatment of autoimmune disease and allergy)

IT Aging, animal
(age effect on thymocyte population; normalization of defective T cell responsiveness through manipulation of thymic regeneration, and use in treatment of autoimmune disease and allergy)

IT Vaccines
(anti-LHRH; normalization of defective T cell responsiveness through manipulation of thymic regeneration, and use in treatment of autoimmune disease and allergy)

IT Androgens
(antiandrogens; normalization of defective T cell responsiveness through manipulation of thymic regeneration, and use in treatment of autoimmune disease and allergy)

IT Estrogens
(antiestrogens; normalization of defective T cell responsiveness through manipulation of thymic regeneration, and use in treatment of autoimmune disease and allergy)

IT Integrins
(antigens Mac-1 (macrophage 1); normalization of defective T cell responsiveness through manipulation of thymic regeneration, and use in treatment of autoimmune disease and allergy)

IT Progestogens
(antiprogestins; normalization of defective T cell responsiveness through manipulation of thymic regeneration, and use in treatment of autoimmune disease and allergy)

IT Transplant and Transplantation
(bone marrow; normalization of defective T cell responsiveness through manipulation of thymic regeneration, and use in treatment of autoimmune disease and allergy)

IT T cell (lymphocyte)
(cytotoxic; normalization of defective T cell responsiveness through manipulation of thymic regeneration, and use in treatment of autoimmune disease and allergy)

IT Lymphocyte
(disease, lymphocytopenia; normalization of defective T cell responsiveness through manipulation of thymic regeneration, and use in

treatment of autoimmune disease and allergy)
IT Estrogen receptors
(downregulators; normalization of defective T cell responsiveness through manipulation of thymic regeneration, and use in treatment of autoimmune disease and allergy)
IT Epithelium
(epithelial stem cell; normalization of defective T cell responsiveness through manipulation of thymic regeneration, and use in treatment of autoimmune disease and allergy)
IT Autoimmune disease
(insulin-dependent diabetes mellitus; normalization of defective T cell responsiveness through manipulation of thymic regeneration, and use in treatment of autoimmune disease and allergy)
IT Diabetes mellitus
(insulin-dependent; normalization of defective T cell responsiveness through manipulation of thymic regeneration, and use in treatment of autoimmune disease and allergy)
IT Blood, disease
(lymphocytopenia; normalization of defective T cell responsiveness through manipulation of thymic regeneration, and use in treatment of autoimmune disease and allergy)
IT Hematopoietic precursor cell
(lymphoid; normalization of defective T cell responsiveness through manipulation of thymic regeneration, and use in treatment of autoimmune disease and allergy)
IT Androgen receptors
(modulators; normalization of defective T cell responsiveness through manipulation of thymic regeneration, and use in treatment of autoimmune disease and allergy)
IT Hematopoietic precursor cell
(myeloid; normalization of defective T cell responsiveness through manipulation of thymic regeneration, and use in treatment of autoimmune disease and allergy)
IT Lymphocyte
(natural killer cell; normalization of defective T cell responsiveness through manipulation of thymic regeneration, and use in treatment of autoimmune disease and allergy)
IT Allergy
IT Allergy inhibitors
IT Autoimmune disease
IT B cell (lymphocyte)
IT CD4-positive T cell
IT CD8-positive T cell
IT Combination chemotherapy
IT Dendritic cell
IT Gene therapy
IT Hematopoietic precursor cell
IT Human
IT Human herpesvirus 1
IT Immunomodulators
IT Immunosuppressants
IT Immunosuppression
IT Lymph node
IT Macrophage
IT Selective estrogen receptor modulators
IT Stem cell
IT T cell (lymphocyte)
IT Thymus gland
IT Transplant and Transplantation
(normalization of defective T cell responsiveness through manipulation of thymic regeneration, and use in treatment of autoimmune disease and allergy)
IT CD3 (antigen)

IT CD34 (antigen)
IT CD4 (antigen)
IT CD44 (antigen)
IT CD45 (antigen)
IT CD45RA (antigen)
IT CD45RO (antigen)
IT CD8 (antigen)
IT TCR (T cell receptors)
(normalization of defective T cell responsiveness through manipulation of thymic regeneration, and use in treatment of autoimmune disease and allergy)
IT Cytokines
IT Growth factors, animal
IT Interleukin 15
IT Interleukin 2
IT Interleukin 7
IT Stem cell factor
IT Thyroid hormones
(normalization of defective T cell responsiveness through manipulation of thymic regeneration, and use in treatment of autoimmune disease and allergy)
IT Signal transduction, biological
(sex steroid-mediated signaling; normalization of defective T cell responsiveness through manipulation of thymic regeneration, and use in treatment of autoimmune disease and allergy)
IT Steroids, biological studies
(sex, sex steroid-mediated signaling; normalization of defective T cell responsiveness through manipulation of thymic regeneration, and use in treatment of autoimmune disease and allergy)
IT Spleen
(splenocyte; normalization of defective T cell responsiveness through manipulation of thymic regeneration, and use in treatment of autoimmune disease and allergy)
IT Sex hormones
(steroidal, sex steroid-mediated signaling; normalization of defective T cell responsiveness through manipulation of thymic regeneration, and use in treatment of autoimmune disease and allergy)
IT Castration
(surgical or chemical; normalization of defective T cell responsiveness through manipulation of thymic regeneration, and use in treatment of autoimmune disease and allergy)
IT Radiation
(thymic atrophy induced by; normalization of defective T cell responsiveness through manipulation of thymic regeneration, and use in treatment of autoimmune disease and allergy)
IT Thymus gland
(thymocyte; normalization of defective T cell responsiveness through manipulation of thymic regeneration, and use in treatment of autoimmune disease and allergy)
IT Bone marrow
(transplant; normalization of defective T cell responsiveness through manipulation of thymic regeneration, and use in treatment of autoimmune disease and allergy)
IT Virus
(virus-specific peripheral T-cell responsiveness; normalization of defective T cell responsiveness through manipulation of thymic regeneration, and use in treatment of autoimmune disease and allergy)
IT Prostate gland, neoplasm
(with chemotherapy; normalization of defective T cell responsiveness through manipulation of thymic regeneration, and use in treatment of autoimmune disease and allergy)
IT Interleukin 2 receptors
(α chain; normalization of defective T cell responsiveness

through manipulation of thymic regeneration, and use in treatment of autoimmune disease and allergy)

IT Integrins
(αX; normalization of defective T cell responsiveness through manipulation of thymic regeneration, and use in treatment of autoimmune disease and allergy)

IT 9039-48-9, Aromatase
(inhibitors; normalization of defective T cell responsiveness through manipulation of thymic regeneration, and use in treatment of autoimmune disease and allergy)

IT 9034-40-6, LHRH
(modulators; normalization of defective T cell responsiveness through manipulation of thymic regeneration, and use in treatment of autoimmune disease and allergy)

IT 646-06-0D, 1,3-Dioxolane, derivs. 9002-72-6, Growth hormone 13311-84-7, Eulexin 33515-09-2, Gonadorelin 34973-08-5, Cystorelin 53714-56-0, Leuprolide 57773-63-4, Triptorelin 57773-65-6, Deslorelin 57982-77-1, Buserelin 61912-98-9, Insulin-like growth factor 62031-54-3, Fibroblast growth factor 62229-50-9, EGF 65277-42-1, Ketoconazole 65807-02-5, Zoladex 66866-63-5, Lutrelin 74381-53-6, Lupron 76712-82-8, Histrelin 76932-56-4, Nafarelin 120287-85-6, Cetrorelix 124508-66-3, Decapeptyl 140703-49-7, Meterelin 143011-72-7, G-CSF 148348-15-6, Fibroblast growth factor 7 183552-38-7, Abarelix
(normalization of defective T cell responsiveness through manipulation of thymic regeneration, and use in treatment of autoimmune disease and allergy)

IT 57-83-0, Progesterone, biological studies
(selective progesterone response modulators; normalization of defective T cell responsiveness through manipulation of thymic regeneration, and use in treatment of autoimmune disease and allergy)

IT 50-18-0, Cyclophosphamide
(thymic atrophy induced by; normalization of defective T cell responsiveness through manipulation of thymic regeneration, and use in treatment of autoimmune disease and allergy)

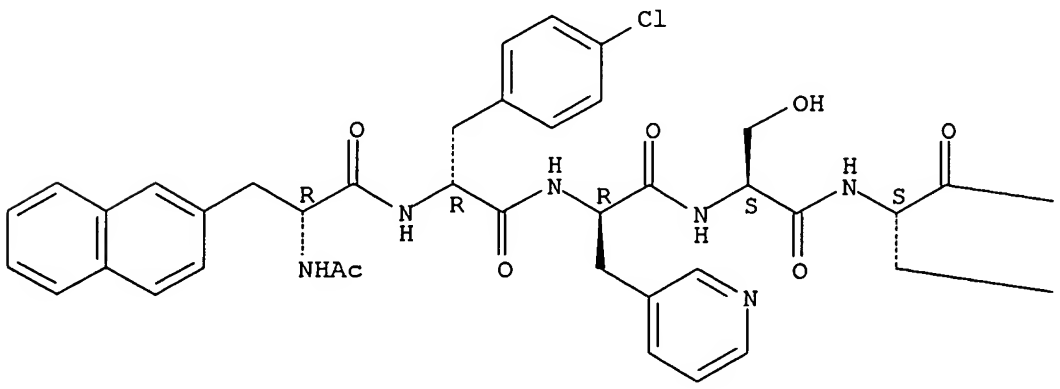
IT 120287-85-6, Cetrorelix
(normalization of defective T cell responsiveness through manipulation of thymic regeneration, and use in treatment of autoimmune disease and allergy)

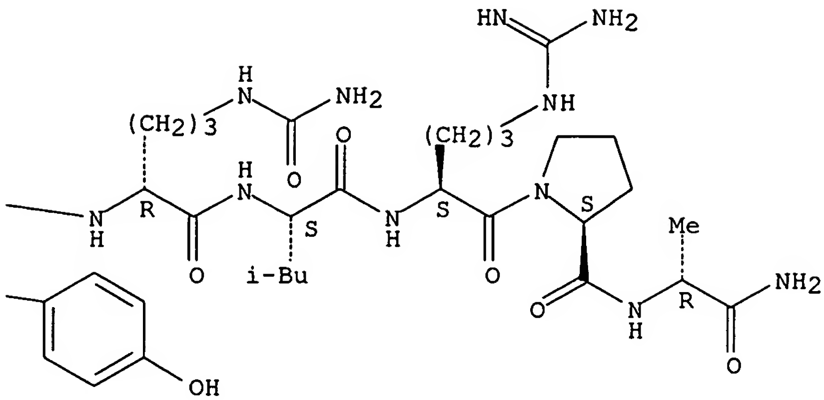
RN 120287-85-6 USPATFULL

CN D-Alaninamide, N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-D-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-L-tyrosyl-N5-(aminocarbonyl)-D-ornithyl-L-leucyl-L-arginyl-L-prolyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A





L15 ANSWER 30 OF 55 USPATFULL on STN

ACCESSION NUMBER: 2004:326853 USPATFULL

TITLE: Graft acceptance through manipulation of thymic regeneration

INVENTOR(S): Boyd, Richard L., Hampton, AUSTRALIA

PATENT ASSIGNEE(S): Monash University (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2004258672	A1	20041223
APPLICATION INFO.:	US 2003-749119	A1	20031230 (10)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 2004-399213, filed on 13 Feb 2004, PENDING A 371 of International Ser. No. WO 2001-AU1291, filed on 15 Oct 2001, UNKNOWN Continuation-in-part of Ser. No. US 2003-419039, filed on 18 Apr 2003, PENDING Continuation-in-part of Ser. No. US 2001-976596, filed on 12 Oct 2001, ABANDONED Continuation-in-part of Ser. No. US 2001-965462, filed on 26 Sep 2001, ABANDONED Continuation-in-part of Ser. No. US 2001-755965, filed on 5 Jan 2001, ABANDONED Continuation-in-part of Ser. No. US 2001-755983, filed on 5 Jan 2001, ABANDONED Continuation-in-part of Ser. No. US 2001-755646, filed on 5 Jan 2001, ABANDONED Continuation-in-part of Ser. No. US 2001-758910, filed on 10 Jan 2001, ABANDONED Continuation-in-part of Ser. No. US 2000-795286, filed on 13 Oct 2000, ABANDONED Continuation-in-part of Ser. No. US 2000-795302, filed on 13 Oct 2000, ABANDONED Continuation-in-part of Ser. No. US 2000-795286, filed on 13 Oct 2000, ABANDONED Continuation-in-part of Ser. No. US 2000-795302, filed on 13 Oct 2000, ABANDONED Continuation-in-part of Ser. No. US 2000-795286, filed on 13 Oct 2000, ABANDONED Continuation-in-part of Ser. No. US 2000-795302, filed on 13 Oct 2000, ABANDONED Continuation-in-part of Ser. No. US 2000-795286, filed on 13 Oct 2000, ABANDONED Continuation-in-part of Ser. No. US 2000-795302, filed on 13 Oct 2000, ABANDONED Continuation-in-part of Ser. No. WO 2000-AU329, filed on 17 Apr 2000, UNKNOWN Continuation-in-part of Ser. No. WO 2000-AU329, filed on 17 Apr 2000, UNKNOWN

NUMBER DATE

PRIORITY INFORMATION:	AU 2000-745	20001013
	AU 1999-9778	19990415
	WO 2000-AU329	20000417
	WO 2002-AU101291	20020418
	US 2003-527001P	20031205 (60)
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	WILMER CUTLER PICKERING HALE AND DORR LLP, 60 STATE STREET, BOSTON, MA, 02109	
NUMBER OF CLAIMS:	56	
EXEMPLARY CLAIM:	CLM-01-18	
NUMBER OF DRAWINGS:	49 Drawing Page(s)	
LINE COUNT:	4112	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present disclosure provides methods for inducing tolerance in a recipient to a mismatched graft of an organ, tissue and/or cells. By reactivating the recipient's thymus and providing hematopoietic stem cells from the donor, the previously "foreign" matter becomes recognized as "self" in the recipient and is not rejected. The patient's T cell population is depleted. In some embodiments, the hematopoietic stem cells are CD34+. The recipient's thymus is reactivated by disruption of sex steroid mediated signaling to the thymus. In some embodiments, this disruption is created by administration of LHRH agonists, LHRH antagonists, anti-LHRH receptor antibodies, anti-LHRH vaccines or combinations thereof.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

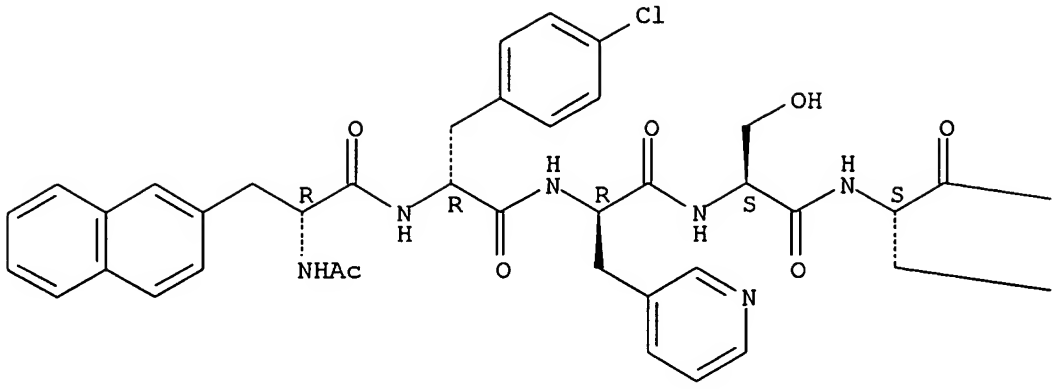
IT Transplant and Transplantation
(allotransplant; graft acceptance through manipulation of thymic regeneration)
IT Vaccines
(anti-LHRH; graft acceptance through manipulation of thymic regeneration)
IT Antibodies and Immunoglobulins
(anti-T cell; graft acceptance through manipulation of thymic regeneration)
IT Androgens
(antiandrogens; graft acceptance through manipulation of thymic regeneration)
IT Estrogens
(antiestrogens; graft acceptance through manipulation of thymic regeneration)
IT Progestogens
(antiprogestins; graft acceptance through manipulation of thymic regeneration)
IT Thymus gland, disease
(atrophy; graft acceptance through manipulation of thymic regeneration)
IT Castration
(chemical; graft acceptance through manipulation of thymic regeneration)
IT B cell (lymphocyte)
(chimeric; graft acceptance through manipulation of thymic regeneration)
IT Growth factors, animal
(epithelial cell growth factors; graft acceptance through manipulation of thymic regeneration)
IT Genetic methods
(genetic modifications; graft acceptance through manipulation of thymic regeneration)
IT Aging, animal
IT Antitumor agents
IT Bone marrow
IT CD4-positive T cell

IT CD8-positive T cell
IT Dendritic cell
IT Drugs
IT Hematopoietic precursor cell
IT Human
IT Human herpesvirus
IT Human herpesvirus 1
IT Immune tolerance
IT Immunity
IT Immunosuppressants
IT Liver
IT Prostate gland, neoplasm
IT Radiotherapy
IT Regeneration, animal
IT Selective estrogen receptor modulators
IT Signal transduction, biological
IT Spleen
IT Stem cell
IT T cell (lymphocyte)
IT Transformation, genetic
IT Transplant and Transplantation
(graft acceptance through manipulation of thymic regeneration)
IT Cell adhesion molecules
IT Estrogen receptors
IT Gonadotropin-releasing hormone receptor
(graft acceptance through manipulation of thymic regeneration)
IT Cytokines
IT Growth factors, animal
IT Interleukin 15
IT Interleukin 2
IT Interleukin 7
IT Stem cell factor
IT Thyroid hormones
(graft acceptance through manipulation of thymic regeneration)
IT Drug delivery systems
(implants; graft acceptance through manipulation of thymic regeneration)
IT Drug delivery systems
(injections; graft acceptance through manipulation of thymic regeneration)
IT Cell migration
(lymphocyte, T cells; graft acceptance through manipulation of thymic regeneration)
IT Organ, animal
(lymphoid, chimeric; graft acceptance through manipulation of thymic regeneration)
IT Hematopoietic precursor cell
(lymphoid; graft acceptance through manipulation of thymic regeneration)
IT Lymphocyte
(migration, T cells; graft acceptance through manipulation of thymic regeneration)
IT Hematopoietic precursor cell
(myeloid; graft acceptance through manipulation of thymic regeneration)
IT Puberty
(post-; graft acceptance through manipulation of thymic regeneration)
IT Thymus gland
(regeneration of; graft acceptance through manipulation of thymic regeneration)
IT Androgen receptors
IT Progesterone receptors
(selective modulators of; graft acceptance through manipulation of thymic regeneration)

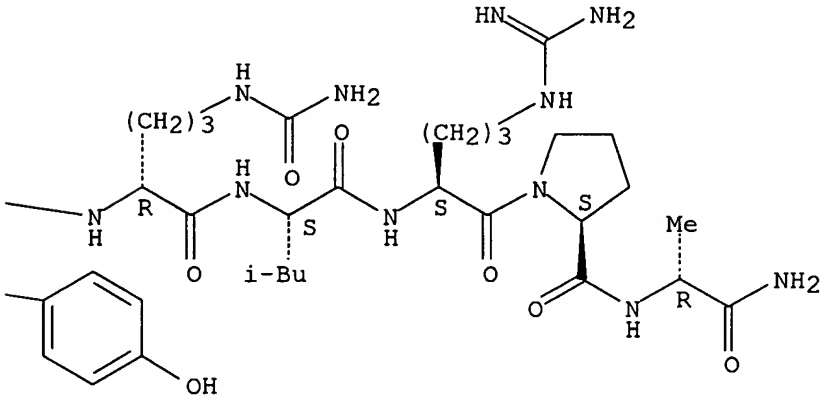
IT Steroids, biological studies
(sex; graft acceptance through manipulation of thymic regeneration)
IT Epithelium
(stem cells; graft acceptance through manipulation of thymic regeneration)
IT Sex hormones
(steroidal; graft acceptance through manipulation of thymic regeneration)
IT Skin
(stratum corneum; graft acceptance through manipulation of thymic regeneration)
IT Surgery
(surgical castration; graft acceptance through manipulation of thymic regeneration)
IT Drug delivery systems
(tablets; graft acceptance through manipulation of thymic regeneration)
IT Cell proliferation
IT Thymus gland
(thymocyte; graft acceptance through manipulation of thymic regeneration)
IT Bone marrow
IT Liver
(toxicity; graft acceptance through manipulation of thymic regeneration)
IT Transplant and Transplantation
(xenotransplant; graft acceptance through manipulation of thymic regeneration)
IT 9039-48-9, Aromatase
(graft acceptance through manipulation of thymic regeneration)
IT 50-18-0, Cyclophosphamide 4362-13-4D, 1,2-Dioxolane, derivs. 9002-72-6, Growth hormone 13311-84-7, Eulexin 33515-09-2, Gonadorelin 34973-08-5, Cystorelin 53714-56-0, Leuprolide 57773-63-4, Triptorelin 57773-65-6, Deslorelin 57982-77-1, Buserelin 62031-54-3, Fibroblast growth factor 65277-42-1, Ketoconazole 65807-02-5, Goserelin 66866-63-5, Lutrelin 67763-96-6, Insulin-like growth factor-1 74381-53-6, Lupron 76712-82-8, Histrelin 76932-56-4, Nafarelin 120287-85-6, Cetrorelix 124508-66-3, Decapeptyl 140703-49-7, Meterelin 143011-72-7, Granulocyte colony stimulating factor 148348-15-6, Fibroblast growth factor 7 183552-38-7, Abarelix
(graft acceptance through manipulation of thymic regeneration)
IT 120287-85-6, Cetrorelix
(graft acceptance through manipulation of thymic regeneration)
RN 120287-85-6 USPATFULL
CN D-Alaninamide, N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-D-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-L-tyrosyl-N5-(aminocarbonyl)-D-ornithyl-L-leucyl-L-arginyl-L-prolyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L15 ANSWER 31 OF 55 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2005400963 EMBASE

TITLE: New developments in the use of peptide gonadotropin -releasing hormone antagonists versus agonists.

AUTHOR: Schultze-Mosgau A.; Griesinger G.; Altgassen C.; von Otte S.; Hornung D.; Diedrich K.

CORPORATE SOURCE: A. Schultze-Mosgau, Medical University of Schleswig-Holstein, Department of Obstetrics and Gynecology, Ratzeburger Allee 160, 23538 Lubeck, Germany. A.Schultze-Mosgau@web.de

SOURCE: Expert Opinion on Investigational Drugs, (2005) Vol. 14, No. 9, pp. 1085-1097. .
Refs: 117
ISSN: 1354-3784 CODEN: EOIDER

COUNTRY: United Kingdom

DOCUMENT TYPE: Journal; General Review

FILE SEGMENT: 016 Cancer
028 Urology and Nephrology
030 Pharmacology
036 Health Policy, Economics and Management
037 Drug Literature Index
038 Adverse Reactions Titles

LANGUAGE: English

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 22 Sep 2005
Last Updated on STN: 22 Sep 2005

AB Gonadotropin-releasing hormone (GnRH) stimulates the pituitary secretion of both luteinising hormone (LH) and follicle-stimulating hormone (FSH), and thus controls the hormonal and reproductive functions of the gonads. The blockade of the effects of GnRH may be sought for a variety of reasons; for example, to control premature LH surges and to reduce the cancellation rate with the aim of improving the pregnancy rate per treatment cycle or in the treatment of sex hormone-dependent disorders. Selective blockade of LH/FSH secretion and subsequent chemical castration have previously been achieved by desensitising the pituitary to continuously administered GnRH or by giving long-acting GnRH agonists. GnRH analogues are indicated for clinical situations in which the suppression of endogenous gonadotropins (precocious puberty, contraception and controlled ovarian hyperstimulation) or sexual steroids (endometriosis, prostate hyperplasia, cancer and uterine fibroids) is desired. The immediate suppression of the pituitary that is achieved by GnRH antagonists without an initial stimulatory effect is the main advantage of these compounds over the agonists. GnRH antagonists have been developed for clinical use with acceptable pharmacokinetic, safety and commercial profiles. In assisted reproduction, these compounds seem to be as effective as established therapy, but with shorter treatment times, less use of gonadotropic hormones, improved patient acceptance, and fewer follicles and oocytes. All of the current indications for GnRH agonist desensitisation may prove to be indications for a GnRH antagonist, including endometriosis, leiomyoma and breast cancer in women, benign prostatic hypertrophy and prostatic carcinoma in men, and central precocious puberty in children. However, the best clinical evidence has been in assisted reproduction and prostate cancer.

L15 ANSWER 32 OF 55 EMBASE

ACCESSION NUMBER: 2001030137 EMBASE
TITLE: GnRH antagonist in single-dose applications.
AUTHOR: Olivennes F.; Fanchin R.; Rongieres-Bertrand C.; Bouchard P.; Frydman R.
CORPORATE SOURCE: Dr. F. Olivennes, Dept. of Obstetrics and Gynecology, A. Beclere Hospital, 157, Rue de la Porte de Trivaux, 92140 Clamart Cedex, France
SOURCE: Infertility and Reproductive Medicine Clinics of North America, (2001) Vol. 12, No. 1, pp. 119-128. .
Refs: 27
ISSN: 1047-9422 CODEN: IRMCF8
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 003 Endocrinology
010 Obstetrics and Gynecology
036 Health Policy, Economics and Management
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 8 Feb 2001
Last Updated on STN: 8 Feb 2001

AB Use of the GnRH antagonist Cetrorelix in natural cycles associated with gonadotropins allowed the authors to reduce the rate of premature and endogenous LH surges and, subsequently, the cancellation rate. Stimulation was minimal, and the pregnancy rates in this preliminary report were satisfactory. If a larger study confirms the results of the natural cycle with hMG support, the association of spontaneous cycles and the GnRH antagonist single-dose

administration could represent in selected indications a promising first-choice IVF treatment regimen, avoiding the complications and the risks of the ovarian stimulation protocols. The reduction of the cost and the benefit of the oocyte retrieval in an outpatient procedure are obvious. Successive cycles with an acceptable success rate could result in increased cumulative pregnancy rates. In controlled ovarian stimulation, different studies have confirmed the efficacy of a single dose of 3 mg of Cetrorelix to prevent premature LH surges when administered in the late follicular phase. The single-dose protocol is easy to use and ensures the patient's compliance. When compared with the long protocol using a depot formula of triptorelin, the IVF-ET results showed a shorter duration of treatment, less amount of hMG needed, and a lower occurrence of ovarian hyperstimulation syndrome. The tolerance to Cetrorelix was excellent in all of the patients treated, with only mild and transitory reactions at the injection site. GnRH antagonists are already available for clinical use in some countries. These compounds are expected to change protocols of ovarian stimulation. If similar pregnancy rates are confirmed, the main advantage of these compounds will be the reduction of side effects and complication rates. They could also allow the design of softer stimulation protocols using clomiphene citrate and "natural cycles." GnRH antagonists will enable different ways of triggering ovulation with native GnRH and GnRH agonists.

L15 ANSWER 33 OF 55 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2006022632 EMBASE
TITLE: Therapeutic strategies for ovulation induction in infertile women with polycystic ovary syndrome.
AUTHOR: Cristello F.; Cela V.; Artini P.G.; Genazzani A.R.
CORPORATE SOURCE: F. Cristello, Department of Reproductive Medicine and Child Development, Division of Obstetrics and Gynecology, University of Pisa, Via Roma 56, I-56126 Pisa, Italy. francesca.cristello@tiscali.it
SOURCE: Gynecological Endocrinology, (2005) Vol. 21, No. 6, pp. 340-352. .
Refs: 103
ISSN: 0951-3590 CODEN: GYENER
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 003 Endocrinology
010 Obstetrics and Gynecology
036 Health Policy, Economics and Management
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 9 Feb 2006
Last Updated on STN: 9 Feb 2006

AB Polycystic ovary syndrome (PCOS) is a heterogeneous disorder characterized by hirsutism, obesity, hyperandrogenism and insulin resistance. The syndrome is often accompanied by infertility because of anovulation. Many approaches have been proposed to solve this problem, with the most commonly used therapies being ovarian drilling and pharmacological ovulation induction. Ovarian drilling is a procedure in which a laser fiber or electro-surgical needle punctures the ovary four to ten times. Side-effects are rare and often related to surgery itself. Pharmacological strategies include administration of metformin and insulin-sensitizing agents, clomiphene citrate (CC), gonadotropins and aromatase inhibitors. Metformin appears valuable in increasing ovulation rate, menstrual cyclicity and pregnancy rate. CC is an oral estrogen antagonist that raises circulating concentrations of follicle-stimulating hormone (FSH)

and induces follicular growth in most women with PCOS and anovulation. Failure to respond is associated with high body mass index and high androgen levels. Aromatase inhibitors mimic the central reduction of negative feedback through which CC works. Ovulation induction with recombinant FSH has proved successful, but treatment requires skill and experience to avoid multiple pregnancies and ovarian hyperstimulation syndrome. The hypothetical deleterious effects of the high luteinizing hormone concentrations observed in PCOS patients seem to be related to the concomitant hyperinsulinemia (and/or insulin resistance). A thorough understanding of the syndrome and a careful assessment of each patient are the mainstays for choosing an appropriate treatment regimen. .COPYRGT. 2005 Taylor & Francis.

L15 ANSWER 34 OF 55 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 2004:259854 BIOSIS
DOCUMENT NUMBER: PREV200400258728
TITLE: Single dose nasal spray of gonadotropin releasing hormone (GnRH) agonist effectively matures oocytes for in vitro fertilization in an ovarian stimulation protocol using clomiphene citrate, gonadotropin, and GnRH antagonist.
AUTHOR(S): Goto, Tetsuya [Reprint Author]; Oka, Chikahiro; Tomiyama, Tatsuhiro; Mukaida, Tetsunori; Takahashi, Katsuhiko
CORPORATE SOURCE: Tokyo HART Clin, Tokyo, Japan
SOURCE: Fertility and Sterility, (September 2003) Vol. 80, No. Suppl. 3, pp. S6. print.
Meeting Info.: 59th Annual Meeting of the American Society for Reproductive Medicine. San Antonio, Texas, USA. October 11-15, 2003. American Society for Reproductive Medicine.
ISSN: 0015-0282 (ISSN print).
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 19 May 2004
Last Updated on STN: 19 May 2004

IT Major Concepts
Gynecology (Human Medicine, Medical Sciences); Pharmacology
IT Parts, Structures, & Systems of Organisms
oocyte: reproductive system
IT Chemicals & Biochemicals
cetrorelix: hormone-drug; cetrotide: hormone-drug; clomiphene citrate: fertility-drug, single dose nasal spray formulation; gonadotropin: fertility-drug, single dose nasal spray formulation; gonadotropin-releasing hormone; gonadotropin-releasing hormone antagonist: contraceptive-drug; human chorionic gonadotropin: hormone-drug, intramuscular administration
IT Methods & Equipment
assisted reproduction: clinical techniques; in vitro fertilization: clinical techniques, therapeutic and prophylactic techniques; ovarian stimulation: clinical techniques, therapeutic and prophylactic techniques
IT Miscellaneous Descriptors
pregnancy
ORGN Classifier
Hominidae 86215
Super Taxa
Primates; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
human (common): patient
Taxa Notes
Animals, Chordates, Humans, Mammals, Primates, Vertebrates

RN 120287-85-6 (cetrorelix)
145672-81-7 (cetrotide)
50-41-9 (clomiphene citrate)
9034-40-6Q (gonadotropin-releasing hormone)
33515-09-2Q (gonadotropin-releasing hormone)
9002-61-3 (human chorionic gonadotropin)

L15 ANSWER 35 OF 55 EMBASE
ACCESSION NUMBER: 2003266622 EMBASE
TITLE: GnRH antagonists in normal-responder patients.
AUTHOR: Shapiro D.B.
CORPORATE SOURCE: Dr. D.B. Shapiro, Reproductive Biology Associates, 1150 Lake Hearn Drive, Atlanta, GA 30342, United States. drshap26@aol.com
SOURCE: Fertility and Sterility, (1 Jul 2003) Vol. 80, No. SUPPL. 1, pp. S8-S15. .
Refs: 15
ISSN: 0015-0282 CODEN: FESTAS
COUNTRY: United States
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 003 Endocrinology
010 Obstetrics and Gynecology
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 17 Jul 2003
Last Updated on STN: 17 Jul 2003
AB Objective: To review the use of GnRH antagonists in normal-responding patients who are undergoing infertility treatment. Design: Review article and case studies. Results: For the normal-responding patient, GnRH antagonist protocols provide equivalent outcomes as GnRH agonist protocols, with the added patient benefit of significantly fewer treatment/injection days. In addition, a decrease or plateau in E(2) on the day after initiation of the GnRH antagonist has no prognostic significance in IVF outcome. Conclusions: For normal-responding patients, a GnRH antagonist can be used in a flexible fashion to achieve high success rates. The lack of correlation between E(2) patterns on the day after initiation of a GnRH antagonist and IVF outcomes supports the concept that no intervention (such as LH add-back) is necessary to guard against an early decrease or plateau during stimulation with recombinant FSH and a GnRH antagonist. Clinicians must consider ovarian physiology and the mechanism of GnRH antagonist action in patient management. .COPYRGT. 2003 by American Society for Reproductive Medicine.

L15 ANSWER 36 OF 55 MEDLINE on STN
ACCESSION NUMBER: 2004614441 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15587144
TITLE: GnRH antagonist improved blastocyst quality and pregnancy outcome after multiple failures of IVF/ICSI-ET with a GnRH agonist protocol.
AUTHOR: Takahashi Katsuhiko; Mukaida Tetsunori; Tomiyama Tatsuhiro; Goto Tetsuya; Oka Chikahiro
CORPORATE SOURCE: Hiroshima HART Clinic, 5-7-10 Ohtemachi, Naka-ku, Hiroshima 730-0051, Japan.. hart@enjoy.ne.jp
SOURCE: Journal of assisted reproduction and genetics, (2004 Sep) Vol. 21, No. 9, pp. 317-22.
Journal code: 9206495. ISSN: 1058-0468.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200503
ENTRY DATE: Entered STN: 20 Dec 2004
Last Updated on STN: 23 Mar 2005
Entered Medline: 22 Mar 2005

AB BACKGROUND: To determine the efficacy of a gonadotrophin-releasing hormone (GnRH) antagonist, cetrorelix, in improving the quality of embryos and pregnancy outcome, we performed a study in patients with a history of multiple failures of in vitro fertilization (IVF) or intracytoplasmic sperm injection (ICSI) cycles with a GnRH agonist (GnRHa) long protocol. METHODS: Forty women with no live births after conventional IVF or ICSI embryo transfer (ET) and subsequent blastocyst transfer (BT) with a GnRHa long protocol entered this study. The treatment protocol consisted of a daily dose of clomiphene citrate 100 mg for 5 days and gonadotrophin injections daily from cycle day 4 onward. Cetrorelix, 0.25 mg/day, was started when the leading follicle reached 14 mm. Induction of ovulation was triggered with human chorionic gonadotrophin (HCG) (N = 36) or GnRHa (N = 4). It was possible to perform BT in 38 patients. RESULTS: Comparison of the results with the results for BT with the previous GnRHa protocol showed no significant differences in number of oocytes retrieved or the zygote- and blastocyst-development rate. With the cetrorelix protocol, however, number of patients whose embryos had developed to at least one expanded blastocyst on day 5 was significantly higher than with the GnRHa protocol (25 vs. 9) ($p < 0.001$), and 16 of the women became pregnant (42.1%), with 7 delivering 9 infants, 4 ending in abortion (25%), and 5 in progressing. CONCLUSIONS: The use of a GnRH antagonist in controlled ovarian hyperstimulation improves the outcome of pregnancy of patients with a history of multiple failure of IVF/ICSI-ET in a GnRHa protocol, most likely due to improvement of the quality of the blastocysts generated.

L15 ANSWER 37 OF 55 EMBASE
ACCESSION NUMBER: 2001352262 EMBASE
TITLE: Is coasting effective for preventing ovarian hyperstimulation syndrome in patients receiving a gonadotropin-releasing hormone antagonist during an in vitro fertilization cycle?.
AUTHOR: Delvigne A.; Carlier C.; Rozenberg S.
CORPORATE SOURCE: Dr. A. Delvigne, IVF Center, Department of Obstetrics, St. Peter Univ. Hospital (ULB-VUB), Rue Haute, 322, 1000 Brussels, Belgium. annick.delvigne@yucom.be
SOURCE: Fertility and Sterility, (2001) Vol. 76, No. 4, pp. 844-846. .
Refs: 6
ISSN: 0015-0282 CODEN: FESTAS
PUBLISHER IDENT.: S 0015-0282(01)02007-6
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 003 Endocrinology
010 Obstetrics and Gynecology
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 25 Oct 2001
Last Updated on STN: 25 Oct 2001

AB Objective: To report two cases of coasting during receipt of GnRH antagonists. Design: Case report. Setting: University hospital. Patient(s): One 27-year-old and one 28-year-old woman, both with risk factors for the ovarian hyperstimulation syndrome (OHSS).

Intervention(s): Two IVF treatments during which hMG treatment was stopped until E(2) decreased to a safer level during receipt of GnRH antagonist. Main Outcome Measure(s): Development of OHSS and pregnancy. Result(s): Embryos were transferred in both women. Neither woman developed OHSS and one ongoing pregnancy was obtained. Conclusion(s): Coasting is feasible when a GnRH antagonist is used during IVF. Further studies are needed to evaluate its preventive role in OHSS. .COPYRGT. 2001 by American Society for Reproductive Medicine.

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ACCESSION NUMBER: 2001030136 EMBASE
TITLE: The use of LHRH agonists to induce ovulation.
AUTHOR: Revel A.; Casper R.F.
CORPORATE SOURCE: Dr. R.F. Casper, 3157, 700 University Avenue, Toronto, Ont. M5G 125, Canada. r.casper@utoronto.ca
SOURCE: Infertility and Reproductive Medicine Clinics of North America, (2001) Vol. 12, No. 1, pp. 105-118. .
Refs: 46
ISSN: 1047-9422 CODEN: IRMCF8
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 003 Endocrinology
010 Obstetrics and Gynecology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 8 Feb 2001
Last Updated on STN: 8 Feb 2001

AB Refinements in controlled ovarian hyperstimulation protocols have increased the effectiveness of ovulation induction and enhanced the ability to recruit multiple mature oocytes for use in ART procedures. OHSS represents a significant complication of ovulation induction, and the prevention of this syndrome is a primary goal. The administration of GnRH agonist instead of hCG to induce the final stages of oocyte maturation and to trigger ovulation has been suggested as a possible preventative measure. This approach takes advantage of the short-acting effect of GnRH agonist on endogenous gonadotropin release and the occurrence of a more physiologic LH and FSH surge. Clinical reports, controlled and uncontrolled, support the effectiveness of GnRH agonist for triggering ovulation, and similar pregnancy rates have been reported when this compound is compared with hCG. The incidence of OHSS may be decreased by the use of GnRH agonist, but larger controlled clinical trials are required to confirm this suggestion. The introduction of GnRH antagonists has led to renewed interest in using GnRH agonist to trigger follicle maturation for IVF and other ART procedures. Randomized controlled studies are being performed to determine efficacy of GnRH agonist induction of ovulation in GnRH antagonist cycles in terms of pregnancy outcome and the prevention of OHSS. Further studies are required to determine the need for luteal phase support in cycles in which GnRH agonist triggers the gonadotropin surge.

L15 ANSWER 39 OF 55 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 2002:178382 BIOSIS
DOCUMENT NUMBER: PREV200200178382
TITLE: Alterations in early follicular LH pulse pattern by the gonadotrophin-releasing hormone (GnRH) antagonist Cetrorelix and subsequent ovarian stimulation with FSH in polycystic ovarian disease (PCOD).
AUTHOR(S): Bals-Pratsch, M. [Reprint author]; Thorsteinsdottir, K. [Reprint author]; Felberbaum, R. [Reprint author]; Ortmann,

O. [Reprint author]; Diedrich, K. [Reprint author]
CORPORATE SOURCE: Women's Hospital, Medical University of Luebeck, Luebeck, Germany
SOURCE: Human Reproduction (Oxford), (2001) Vol. 16, No. Abstract Book 1, pp. 209. print.
Meeting Info.: 17th Annual Meeting of the European Society of Human Reproduction and Embryology. Lausanne, Switzerland. July 01-04, 2001. European Society of Human Reproduction and Embryology; European Society of Human Reproduction and Embryology.
CODEN: HUREEE. ISSN: 0268-1161.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
Conference; (Meeting Poster)
LANGUAGE: English
ENTRY DATE: Entered STN: 6 Mar 2002
Last Updated on STN: 6 Mar 2002
IT Major Concepts
Gynecology (Human Medicine, Medical Sciences); Pharmacology
IT Parts, Structures, & Systems of Organisms
blood: blood and lymphatics
IT Diseases
female infertility: reproductive system disease/female, therapy
Infertility, Female (MeSH)
IT Diseases
polycystic ovarian disease: endocrine disease/gonads, reproductive system disease/female, PCOD
Polycystic Ovary Syndrome (MeSH)
IT Chemicals & Biochemicals
Cetrorelix: fertility-drug, hormone-drug, gonadotrophin-releasing hormone antagonist; FSH: fertility-drug, hormone-drug; LH [luteinizing hormone]; androgen; clomiphene: fertility-drug
IT Methods & Equipment
ovarian stimulation: assisted reproduction method
IT Miscellaneous Descriptors
drug efficacy; drug safety; early follicular LH pulse pattern [early follicular luteinizing hormone pulse pattern]; Meeting Abstract; Meeting Poster
ORGN Classifier
Hominidae 86215
Super Taxa
Primates; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
human: adult, female, patient
Taxa Notes
Animals, Chordates, Humans, Mammals, Primates, Vertebrates
RN 120287-85-6 (Cetrorelix)
9002-68-0 (FSH)
911-45-5 (clomiphene)
9002-67-9 (LUTEINIZING HORMONE)

L15 ANSWER 40 OF 55 MEDLINE on STN
ACCESSION NUMBER: 1998427993 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9755411
TITLE: New approaches to ovarian stimulation.
AUTHOR: Diedrich K; Felberbaum R
CORPORATE SOURCE: Department of Obstetrics and Gynecology, Medical University of Lubeck, Germany.
SOURCE: Human reproduction (Oxford, England), (1998 Jun) Vol. 13 Suppl 3, pp. 1-13; discussion 14-7. Ref: 43
Journal code: 8701199. ISSN: 0268-1161.

PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199811
ENTRY DATE: Entered STN: 6 Jan 1999
Last Updated on STN: 6 Jan 1999
Entered Medline: 17 Nov 1998

AB Suppression of endogenous hormone production by gonadotrophin-releasing hormone (GnRH) agonists followed by controlled ovarian hyperstimulation (COH) with human gonadotrophins, especially the so-called 'long protocol' has developed from second-line into first-line therapy. Due to this attitude premature luteinization can be safely avoided, enhancing therapeutic efficacy. Recombinant preparations of human follicle stimulating hormone (FSH) have been proven to be effective within COH according to the long protocol. The high purity of these compounds may have clinical advantages. GnRH antagonists could be successfully introduced in COH protocols. Also, daily injections in the midcycle phase according to the 'Lubeck protocol', as single or only dual administrations around day 9 seem to abolish any premature LH rises. Due to their different pharmacological mode of action, based on a classic competitive receptor blockage GnRH antagonists avoid any flare-up period and allow ovarian stimulation to start within the spontaneous cycle. Pregnancy rates are comparable to those after long protocol stimulation. Combination of softer stimulation regimes like clomiphene citrate and low dose HMG with midcycle administration of GnRH antagonists may be the way to a cheap, safe and efficient ovarian stimulation. It seems to be high time for modest forms of ovarian stimulation, lowering burden and risk for our patients.

L15 ANSWER 41 OF 55 USPATFULL on STN
ACCESSION NUMBER: 2001:131288 USPATFULL
TITLE: Method of treatment for uterine leiomyoma
INVENTOR(S): Katsuki, Yukio, Tokyo, Japan
Shimora, Minoru, Tokyo, Japan
PATENT ASSIGNEE(S): Mochida Pharmaceutical Co., Ltd., Tokyo, Japan
(non-U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6274573	B1	20010814	
	WO 9920647		19990429	
APPLICATION INFO.:	US 2000-529640		20000417	(9)
	WO 1998-JP4691		19981016	
			20000417	PCT 371 date
			20000417	PCT 102(e) date

	NUMBER	DATE
PRIORITY INFORMATION:	JP 1997-285826	19971017

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Weber, Jon P.
ASSISTANT EXAMINER: Patten, Patricia D
LEGAL REPRESENTATIVE: Birch, Stewart, Kolasch & Birch, LLP
NUMBER OF CLAIMS: 11
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 1 Drawing Figure(s); 1 Drawing Page(s)
LINE COUNT: 471
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Providing a therapeutic agent of uterine leiomyoma, containing dienogest and a solvate thereof as the effective ingredient with less adverse

effects, which can be used either singly or in combination with GnRH and can be administered or pharmaceutically manufactured as oral, transdermal dosing agents or suppositories.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT Capsules (drug delivery systems)
IT Suppositories (drug delivery systems)
IT Tablets (drug delivery systems)
(hysteromyoma remedy containing dienogest as the active ingredient)
IT Uterine diseases
(hysteromyoma; hysteromyoma remedy containing dienogest as the active ingredient)
IT 9034-40-6, GnRH
(agonists; hysteromyoma remedy containing dienogest as the active ingredient)
IT 65928-58-7, Dienogest
(hysteromyoma remedy containing dienogest as the active ingredient)

L15 ANSWER 42 OF 55 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 2005:305193 BIOSIS
DOCUMENT NUMBER: PREV200510089022
TITLE: In vitro fertilization surrogate pregnancy in a patient who underwent radical hysterectomy followed by ovarian transposition, lower abdominal wall radiotherapy, and chemotherapy.
AUTHOR(S): Steigrad, Stephen [Reprint Author]; Hacker, Neville F.; Kolb, Bradford
CORPORATE SOURCE: Royal Hosp Women, Dept Reprod Med, Randwick, NSW, Australia
SOURCE: Fertility and Sterility, (MAY 2005) Vol. 83, No. 5, pp. 1547.
CODEN: FESTAS. ISSN: 0015-0282.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 15 Aug 2005
Last Updated on STN: 15 Aug 2005
IT Major Concepts
Pharmacology; Oncology (Human Medicine, Medical Sciences); Gynecology (Human Medicine, Medical Sciences)
IT Diseases
miscarriage: reproductive system disease/female
Abortion, Spontaneous (MeSH)
IT Diseases
premature ovarian failure: reproductive system disease/female, endocrine disease/gonads
Ovarian Failure, Premature (MeSH)
IT Chemicals & Biochemicals
clomiphene citrate: fertility-drug; FSH: fertility-drug; cetrorelix acetate: fertility -drug
IT Methods & Equipment
chemotherapy: therapeutic and prophylactic techniques, clinical techniques; cryopreservation: laboratory techniques; radiotherapy: therapeutic and prophylactic techniques, clinical techniques; in vitro fertilization: clinical techniques; radical hysterectomy: therapeutic and prophylactic techniques, clinical techniques; ovarian transposition: clinical techniques
IT Miscellaneous Descriptors
surrogate pregnancy
RN 50-41-9 (clomiphene citrate)
9002-68-0 (FSH)
145672-81-7 (cetrorelix acetate)

L15 ANSWER 43 OF 55 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 2000:457980 BIOSIS
DOCUMENT NUMBER: PREV200000457980
TITLE: Ovarian stimulation in poor responders using GnRH antagonists.
AUTHOR(S): Nikolettos, N. [Reprint author]; Al-Hasani, S.; Felberbaum, R.; Kupker, W.; Schopper, B.; Sturm, R.; Diedrich, K.
CORPORATE SOURCE: Faculty of Medicine, Democritus University of Thrace, Alexandroupolis, Greece
SOURCE: Human Reproduction (Oxford), (June, 2000) Vol. 15, No. Abstract Book 1, pp. 125. print.
Meeting Info.: 16th Annual Meeting of the European Society of Human Reproduction and Embryology. Bologna, Italy. June 25-28, 2000. European Society of Human Reproduction and Embryology.
CODEN: HUREEE. ISSN: 0268-1161.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 25 Oct 2000
Last Updated on STN: 10 Jan 2002
IT Major Concepts
Gynecology (Human Medicine, Medical Sciences); Obstetrics (Human Medicine, Medical Sciences); Pharmacology
IT Parts, Structures, & Systems of Organisms
oocyte: reproductive system; ovary: reproductive system
IT Chemicals & Biochemicals
Cetrorelix: fertility-drug, Luebeck's multiple-dose protocol; Cetrotide: fertility-drug, GnRH antagonist, multiple dose scheduling, standard long protocol; GnRH antagonists: fertility; HMG: fertility -drug, hormone-drug; clomiphene citrate: fertility -drug, GnRH antagonist; estradiol; gonadotrophins: fertility, hormone
IT Methods & Equipment
ICSI [intracytoplasmic sperm injection]: assisted reproduction method; embryo transfer: assisted reproduction method; ovarian stimulation: assisted reproduction method
IT Miscellaneous Descriptors
poor response novel treatment approach; pregnancy rate; Meeting Abstract
ORGN Classifier
Hominidae 86215
Super Taxa
Primates; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
human: embryo, female, patient, poor responder
Taxa Notes
Animals, Chordates, Humans, Mammals, Primates, Vertebrates
RN 120287-85-6 (Cetrorelix)
145672-81-7 (Cetrotide)
50-41-9 (clomiphene citrate)
50-28-2 (estradiol)

L15 ANSWER 44 OF 55 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 2004403189 EMBASE
TITLE: [Inhibins in woman's hypofertility: Practical interest]. LES INHIBINES DANS L'HYPOFERTILITE FEMININE: LEUR APPORT POUR LA PRATIQUE.
AUTHOR: Coussieu C.
CORPORATE SOURCE: christiane.coussieu@htd.ap-hop-paris.fr

SOURCE: Gynecologie Obstetrique Fertilite, (2004) Vol. 32, No. 9, pp. 760-766. .
Refs: 44
ISSN: 1297-9589 CODEN: GOFEF4
PUBLISHER IDENT.: S 1297-9589(04)00230-9
COUNTRY: France
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 010 Obstetrics and Gynecology
037 Drug Literature Index
LANGUAGE: French
SUMMARY LANGUAGE: English; French
ENTRY DATE: Entered STN: 7 Oct 2004
Last Updated on STN: 7 Oct 2004

AB Inhibin B measurement is evolving as a very common prescription in woman's hypofertility diagnosis and follow-up. The aim of this short review of literature is to assess the pertinence of addition of this parameter in the evaluation of the ovarian reserve and in the follow-up of the ovary stimulation treatments. Many studies have been conducted but their results are controversial. According to a majority of authors, inhibin B assay does not systematically bring a discriminant input in borderline clinic cases, already documented by age, plasmatic FSH or even plasmatic estradiol, and echographic evaluation of number of antral follicles on day 3. Most recent publications however grant a growing positive interest in the inhibin B inclusion in the EFORT test as it allows to notably improve the evaluation of the ovarian reserve. Plasma inhibin B assay during the stimulation protocols does not seem to bring significant complementary information and, in any event, cannot be routinely prescribed for a therapeutic follow-up as long as there is no available rapid inhibin assay. Inhibin A evaluation is only performed in research protocols. Research developments regarding the regulation of the post-transfer luteal phase and the implantation mechanisms are still required to evaluate the accuracy of inhibin A as a marker of this still unknown stage. .COPYRGT. 2004 Publie par Elsevier SAS.

L15 ANSWER 45 OF 55 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 2000:458014 BIOSIS
DOCUMENT NUMBER: PREV200000458014
TITLE: GnRH antagonists, an asset in a soft protocol of ovarian stimulation.
AUTHOR(S): Zhioua, F. [Reprint author]; Mahmoud, K.; Ben Aribia, H.; Zhioua, A. [Reprint author]; Hachicha, R. [Reprint author]; Meriah, S. [Reprint author]
CORPORATE SOURCE: Service de Gynecologie-Obstetrique et de Reproduction Humaine, l'Hopital Aziza Ottirnana, Tunis, Tunisia
SOURCE: Human Reproduction (Oxford), (June, 2000) Vol. 15, No. Abstract Book 1, pp. 139. print.
Meeting Info.: 16th Annual Meeting of the European Society of Human Reproduction and Embryology. Bologna, Italy. June 25-28, 2000. European Society of Human Reproduction and Embryology.
CODEN: HUREEE. ISSN: 0268-1161.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 25 Oct 2000
Last Updated on STN: 10 Jan 2002

IT Major Concepts
Obstetrics (Human Medicine, Medical Sciences); Pharmacology
IT Diseases
ovarian hyperstimulation syndrome: endocrine disease/gonads, reproductive system disease/female
Ovarian Hyperstimulation Syndrome (MeSH)

IT Chemicals & Biochemicals
Cetrorelix [Cetrotride R]: fertility-drug; GnRH antagonists [GnRHa]: fertility, hormone; Triptorelin: fertility-drug; clomiphene citrate: fertility -drug; human menopausal gonadotropin: fertility -drug, hormone-drug; recombinant FSH [rFSH]: fertility-drug, hormone-drug
IT Methods & Equipment
IVF [in-vitro fertilization]: assisted reproduction method; embryo transfer [ET]: assisted reproduction method; ovarian stimulation protocol: assisted reproduction method, soft protocol
IT Miscellaneous Descriptors
Meeting Abstract
ORGN Classifier
Hominidae 86215
Super Taxa
Primates; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
human: female, patient
Taxa Notes
Animals, Chordates, Humans, Mammals, Primates, Vertebrates
RN 120287-85-6 (Cetrorelix)
120287-85-6 (Cetrotride R)
57773-63-4 (Triptorelin)
50-41-9 (clomiphene citrate)
61489-71-2 (human menopausal gonadotropin)

L15 ANSWER 46 OF 55 USPATFULL on STN
ACCESSION NUMBER: 2004:145017 USPATFULL
TITLE: Methods for treating hormone associated conditions using a combination of LHRH antagonists and specific estrogen receptor modulators
INVENTOR(S): Garnick, Marc B., Brookline, MA, UNITED STATES
PATENT ASSIGNEE(S): Praecis Pharmaceuticals, Inc., Waltham, MA (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2004110689	A1	20040610
APPLICATION INFO.:	US 2003-619684	A1	20030714 (10)

RELATED APPLN. INFO.: Continuation of Ser. No. WO 2002-US751, filed on 9 Jan 2002, PENDING

	NUMBER	DATE
PRIORITY INFORMATION:	US 2001-262494P	20010117 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: LAHIVE & COCKFIELD, LLP., 28 STATE STREET, BOSTON, MA, 02109
NUMBER OF CLAIMS: 46
EXEMPLARY CLAIM: 1
LINE COUNT: 1170
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Methods for treating hormone associated conditions, such as endometriosis, uterine leiomata, ovarian cancer, breast cancer, or vaginal bleeding, using LHRH antagonists and selective estrogen receptor modulators are disclosed. The methods include administering to a subject a combination of an LHRH antagonist and a selective estrogen receptor modulator. Pharmaceutical compositions and kits for use in the methods of the invention are also provided.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT Leukemia
(acute myelogenous; treating hormone-associated conditions using combination of LHRH antagonists and specific estrogen receptor modulators)
IT Vagina
(bleeding, thrombocytopenia-associated; treating hormone-associated conditions using combination of LHRH antagonists and specific estrogen receptor modulators)
IT Peptides, biological studies
(decapeptides; treating hormone-associated conditions using combination of LHRH antagonists and specific estrogen receptor modulators)
IT Platelet (blood)
(disease, thrombocytopenia, vaginal bleeding due to; treating hormone-associated conditions using combination of LHRH antagonists and specific estrogen receptor modulators)
IT Uterus, disease
(endometriosis; treating hormone-associated conditions using combination of LHRH antagonists and specific estrogen receptor modulators)
IT Myoma
(leiomyoma, uterine; treating hormone-associated conditions using combination of LHRH antagonists and specific estrogen receptor modulators)
IT Uterus, neoplasm
(leiomyoma; treating hormone-associated conditions using combination of LHRH antagonists and specific estrogen receptor modulators)
IT Peptides, biological studies
(nonapeptides; treating hormone-associated conditions using combination of LHRH antagonists and specific estrogen receptor modulators)
IT Ovary, disease
(polycystic; treating hormone-associated conditions using combination of LHRH antagonists and specific estrogen receptor modulators)
IT Ovarian cycle
(premenstrual syndrome; treating hormone-associated conditions using combination of LHRH antagonists and specific estrogen receptor modulators)
IT Drug delivery systems
(sustained-release; treating hormone-associated conditions using combination of LHRH antagonists and specific estrogen receptor modulators)
IT Antitumor agents
IT Disease, animal
IT Human
IT Mammary gland, neoplasm
IT Ovary, neoplasm
(treating hormone-associated conditions using combination of LHRH antagonists and specific estrogen receptor modulators)
IT Estrogen receptors
IT Estrogens
IT Hormones, animal, biological studies
(treating hormone-associated conditions using combination of LHRH antagonists and specific estrogen receptor modulators)
IT Hemorrhage
(uterine; treating hormone-associated conditions using combination of LHRH antagonists and specific estrogen receptor modulators)
IT 9034-40-6, LHRH
(antagonists; treating hormone-associated conditions using combination of LHRH antagonists and specific estrogen receptor modulators)
IT 9034-40-6D, LHRH, analogs 10540-29-1, Tamoxifen 84449-90-1, Raloxifene 183552-38-7 186835-68-7
(treating hormone-associated conditions using combination of LHRH antagonists and specific estrogen receptor modulators)

L15 ANSWER 47 OF 55 USPATFULL on STN

ACCESSION NUMBER: 2005:298540 USPATFULL
TITLE: Anti-IL-9 antibody formulations and uses thereof
INVENTOR(S): Allan, Christian B., Brookeville, MD, UNITED STATES
PATENT ASSIGNEE(S): MedImmune, Inc. (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2005260204	A1	20051124
APPLICATION INFO.:	US 2005-105268	A1	20050412 (11)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2004-561845P	20040412 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: JONES DAY, 222 EAST 41ST ST, NEW YORK, NY, 10017, US
NUMBER OF CLAIMS: 105
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 18 Drawing Page(s)
LINE COUNT: 9913
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention provides liquid formulations of antibodies or antibody fragments that immunospecifically bind to an IL-9 polypeptide, which formulations exhibit stability, low to undetectable levels of aggregation, and very little to no loss of the biological activities of the antibodies or antibody fragments, even during long periods of storage. In particular, the present invention provides liquid formulations of antibodies or fragments thereof that immunospecifically bind to an IL-9 polypeptide, which formulations are substantially free of surfactants, sugars, sugar alcohols, amino acids other than histidine (preferably with pKa values of less than 5 and above 7), and/or other common excipients. Furthermore, the invention provides methods of preventing, treating or ameliorating a disease or disorder associated with or characterized by aberrant expression and/or activity of an IL-9 polypeptide, a disease or disorder associated with or characterized by aberrant expression and/or activity of the IL-9R or one or more subunits thereof, an autoimmune disease, an inflammatory disease, a proliferative disease, or an infection (preferably, a respiratory infection), or one or more symptoms thereof, utilizing the liquid formulations of the present invention.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT Surfactants
(-free formulations; anti-interleukin 9 (IL-9) antibody formulations for treating IL-9- or IL-9R-associated disorders)
IT Alditols
IT Carbohydrates, biological studies
IT Salts, biological studies
(-free formulations; anti-interleukin 9 (IL-9) antibody formulations for treating IL-9- or IL-9R-associated disorders)
IT pH
(5.0-7.0; anti-interleukin 9 (IL-9) antibody formulations for treating IL-9- or IL-9R-associated disorders)
IT High-performance gel-permeation chromatography
(HPSEC (high performance size exclusion chromatog.), stability determined by; anti-interleukin 9 (IL-9) antibody formulations for treating IL-9- or IL-9R-associated disorders)
IT Drug delivery systems
(aerosols; anti-interleukin 9 (IL-9) antibody formulations for treating IL-9- or IL-9R-associated disorders)
IT Allergy
IT Allergy inhibitors
IT Anti-infective agents

IT Anti-inflammatory agents
IT Antiasthmatics
IT Antidiabetic agents
IT Asthma
IT Autoimmune disease
IT Cardiovascular agents
IT Combination chemotherapy
IT Dermatomyositis
IT Diabetes mellitus
IT Human
IT Inflammation
IT Multiple sclerosis
IT Prophylaxis
IT Rheumatoid arthritis
(anti-interleukin 9 (IL-9) antibody formulations for treating IL-9- or IL-9R-associated disorders)
IT Interleukin 9
(anti-interleukin 9 (IL-9) antibody formulations for treating IL-9- or IL-9R-associated disorders)
IT Antibodies and Immunoglobulins
(anti-interleukin 9 (IL-9) antibody formulations for treating IL-9- or IL-9R-associated disorders)
IT Storage
(antibody retains activity during; anti-interleukin 9 (IL-9) antibody formulations for treating IL-9- or IL-9R-associated disorders)
IT Standard substances, analytical
(antibody, comparison to; anti-interleukin 9 (IL-9) antibody formulations for treating IL-9- or IL-9R-associated disorders)
IT Physiological saline solutions
(as carrier; anti-interleukin 9 (IL-9) antibody formulations for treating IL-9- or IL-9R-associated disorders)
IT Oligosaccharides, biological studies
IT Polysaccharides, biological studies
(as excipient; anti-interleukin 9 (IL-9) antibody formulations for treating IL-9- or IL-9R-associated disorders)
IT Adrenal gland, disease
(autoimmune adrenal insufficiency; anti-interleukin 9 (IL-9) antibody formulations for treating IL-9- or IL-9R-associated disorders)
IT Autoimmune disease
IT Inflammation
IT Thyroid gland, disease
(autoimmune thyroiditis; anti-interleukin 9 (IL-9) antibody formulations for treating IL-9- or IL-9R-associated disorders)
IT Heart, disease
IT Inflammation
(carditis, rheumatoid; anti-interleukin 9 (IL-9) antibody formulations for treating IL-9- or IL-9R-associated disorders)
IT Drug delivery systems
(carriers; anti-interleukin 9 (IL-9) antibody formulations for treating IL-9- or IL-9R-associated disorders)
IT Inflammation
(chronic; anti-interleukin 9 (IL-9) antibody formulations for treating IL-9- or IL-9R-associated disorders)
IT Anti-inflammatory agents
(combination therapy with other; anti-interleukin 9 (IL-9) antibody formulations for treating IL-9- or IL-9R-associated disorders)
IT Angiogenesis inhibitors
IT Antitumor agents
IT Immunomodulators
(combination therapy with; anti-interleukin 9 (IL-9) antibody formulations for treating IL-9- or IL-9R-associated disorders)
IT Medical goods
(containers; anti-interleukin 9 (IL-9) antibody formulations for

treating IL-9- or IL-9R-associated disorders)
IT Antibodies and Immunoglobulins
(fragments; anti-interleukin 9 (IL-9) antibody formulations for treating IL-9- or IL-9R-associated disorders)
IT Drug delivery systems
(freeze-dried; anti-interleukin 9 (IL-9) antibody formulations for treating IL-9- or IL-9R-associated disorders)
IT Respiratory system, disease
(infection; anti-interleukin 9 (IL-9) antibody formulations for treating IL-9- or IL-9R-associated disorders)
IT Tumor necrosis factors
(inhibitors, combination therapy with; anti-interleukin 9 (IL-9) antibody formulations for treating IL-9- or IL-9R-associated disorders)
IT Drug delivery systems
(injections, i.m.; anti-interleukin 9 (IL-9) antibody formulations for treating IL-9- or IL-9R-associated disorders)
IT Drug delivery systems
(injections, i.v.; anti-interleukin 9 (IL-9) antibody formulations for treating IL-9- or IL-9R-associated disorders)
IT Drug delivery systems
(injections, s.c.; anti-interleukin 9 (IL-9) antibody formulations for treating IL-9- or IL-9R-associated disorders)
IT Interleukin receptors
(interleukin 9; anti-interleukin 9 (IL-9) antibody formulations for treating IL-9- or IL-9R-associated disorders)
IT Containers
(medical; anti-interleukin 9 (IL-9) antibody formulations for treating IL-9- or IL-9R-associated disorders)
IT Bone
(metabolism, regulating agents, combination therapy with; anti-interleukin 9 (IL-9) antibody formulations for treating IL-9- or IL-9R-associated disorders)
IT Antibodies and Immunoglobulins
(monoclonal, 4D4; anti-interleukin 9 (IL-9) antibody formulations for treating IL-9- or IL-9R-associated disorders)
IT Antibodies and Immunoglobulins
(monoclonal, 4D4H2-1-D11; anti-interleukin 9 (IL-9) antibody formulations for treating IL-9- or IL-9R-associated disorders)
IT Antibodies and Immunoglobulins
(monoclonal, 4D4com-2F9; anti-interleukin 9 (IL-9) antibody formulations for treating IL-9- or IL-9R-associated disorders)
IT Antibodies and Immunoglobulins
(monoclonal, 4D4com-XF-9; anti-interleukin 9 (IL-9) antibody formulations for treating IL-9- or IL-9R-associated disorders)
IT Antibodies and Immunoglobulins
(monoclonal, 71A10; anti-interleukin 9 (IL-9) antibody formulations for treating IL-9- or IL-9R-associated disorders)
IT Antibodies and Immunoglobulins
(monoclonal, 7F3-22D3; anti-interleukin 9 (IL-9) antibody formulations for treating IL-9- or IL-9R-associated disorders)
IT Antibodies and Immunoglobulins
(monoclonal, 7F3; anti-interleukin 9 (IL-9) antibody formulations for treating IL-9- or IL-9R-associated disorders)
IT Antibodies and Immunoglobulins
(monoclonal, 7F3com-2H2; anti-interleukin 9 (IL-9) antibody formulations for treating IL-9- or IL-9R-associated disorders)
IT Antibodies and Immunoglobulins
(monoclonal, 7F3com-3D4; anti-interleukin 9 (IL-9) antibody formulations for treating IL-9- or IL-9R-associated disorders)
IT Antibodies and Immunoglobulins
(monoclonal, 7F3com-3H5; anti-interleukin 9 (IL-9) antibody formulations for treating IL-9- or IL-9R-associated disorders)
IT Antibodies and Immunoglobulins

(monoclonal, Mab fragment; anti-interleukin 9 (IL-9) antibody formulations for treating IL-9- or IL-9R-associated disorders)

IT Drug delivery systems
(nasal, intra-; anti-interleukin 9 (IL-9) antibody formulations for treating IL-9- or IL-9R-associated disorders)

IT Drug delivery systems
(oral; anti-interleukin 9 (IL-9) antibody formulations for treating IL-9- or IL-9R-associated disorders)

IT Amino acids, biological studies
(other than histidine, formulations free from; anti-interleukin 9 (IL-9) antibody formulations for treating IL-9- or IL-9R-associated disorders)

IT Drug delivery systems
(parenterals; anti-interleukin 9 (IL-9) antibody formulations for treating IL-9- or IL-9R-associated disorders)

IT Alcohols, biological studies
(polyhydric, as excipient; anti-interleukin 9 (IL-9) antibody formulations for treating IL-9- or IL-9R-associated disorders)

IT Sjogren's syndrome
(polymyositis; anti-interleukin 9 (IL-9) antibody formulations for treating IL-9- or IL-9R-associated disorders)

IT Anemia (disease)
(pure red cell; anti-interleukin 9 (IL-9) antibody formulations for treating IL-9- or IL-9R-associated disorders)

IT Infection
(respiratory tract; anti-interleukin 9 (IL-9) antibody formulations for treating IL-9- or IL-9R-associated disorders)

IT Connective tissue, disease
(scleroderma; anti-interleukin 9 (IL-9) antibody formulations for treating IL-9- or IL-9R-associated disorders)

IT Lupus erythematosus
(systemic; anti-interleukin 9 (IL-9) antibody formulations for treating IL-9- or IL-9R-associated disorders)

IT 50-99-7, Dextrose, biological studies
(5% dextrose in water (D5W), as carrier; anti-interleukin 9 (IL-9) antibody formulations for treating IL-9- or IL-9R-associated disorders)

IT 7732-18-5, Water, biological studies
(distilled, as carrier; anti-interleukin 9 (IL-9) antibody formulations for treating IL-9- or IL-9R-associated disorders)

IT 7647-14-5, Sodium chloride, biological studies
(formulation comprising; anti-interleukin 9 (IL-9) antibody formulations for treating IL-9- or IL-9R-associated disorders)

IT 56-40-6, Glycine, biological studies 71-00-1, Histidine, biological studies
(in formulation; anti-interleukin 9 (IL-9) antibody formulations for treating IL-9- or IL-9R-associated disorders)

IT 869906-89-8 869906-90-1 869906-91-2 869906-92-3 869906-93-4
869906-94-5 869906-95-6 869906-96-7 869906-97-8 869907-01-7
869907-02-8 869907-03-9
(unclaimed nucleotide sequence; anti-interleukin 9 (IL-9) antibody formulations for treating IL-9- or IL-9R-associated disorders)

IT 869906-70-7 869906-71-8 869906-72-9 869906-73-0 869906-74-1
869906-75-2 869906-76-3 869906-77-4 869906-78-5 869906-79-6
869906-80-9 869906-81-0 869906-82-1 869906-83-2 869906-84-3
869906-85-4 869906-86-5 869906-87-6 869906-88-7 869906-98-9
869906-99-0 869907-00-6 869907-04-0 869907-05-1 869907-06-2
(unclaimed protein sequence; anti-interleukin 9 (IL-9) antibody formulations for treating IL-9- or IL-9R-associated disorders)

IT 145060-92-0 145060-93-1 145061-00-3 158512-03-9 208518-20-1
246223-11-0 246223-20-1 728944-79-4 784200-47-1 784200-48-2
784200-49-3 784200-50-6 784200-51-7 784200-52-8 784200-53-9
784200-54-0 784200-55-1 784200-56-2 784200-57-3 784200-58-4
784200-59-5 784200-60-8 784200-61-9

(unclaimed sequence; anti-interleukin 9 (IL-9) antibody formulations for treating IL-9- or IL-9R-associated disorders)

L15 ANSWER 48 OF 55 USPATFULL on STN

ACCESSION NUMBER:	2004:267333 USPATFULL		
TITLE:	Stabilized high concentration anti-integrin alphanubeta3 antibody formulations		
INVENTOR(S):	Allan, Christian B., Brookeville, MD, UNITED STATES		
PATENT ASSIGNEE(S):	MedImmune, Inc. (U.S. corporation)		
	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2004208870	A1	20041021
APPLICATION INFO.:	US 2004-769712	A1	20040130 (10)
	NUMBER		DATE
PRIORITY INFORMATION:	US 2003-443777P		20030130 (60)
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	APPLICATION		
LEGAL REPRESENTATIVE:	JONES DAY, 222 EAST 41ST ST, NEW YORK, NY, 10017		
NUMBER OF CLAIMS:	55		
EXEMPLARY CLAIM:	1		
NUMBER OF DRAWINGS:	1 Drawing Page(s)		
LINE COUNT:	6217		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention provides liquid formulations of antibodies or antibody fragments that immunospecifically bind to integrin α.sub.Vβ.sub.3, which formulations exhibit stability, low to undetectable levels of aggregation, and very little to no loss of the biological activities of the antibodies or antibody fragments, even during long periods of storage. In particular, the present invention provides liquid formulations of antibodies or fragments thereof that immunospecifically bind to integrin α.sub.Vβ.sub.3, which formulations are substantially free of surfactant, inorganic salts, and/or other common excipients. Furthermore, the invention provides methods of preventing, treating or ameliorating an inflammatory disorder, an autoimmune disorder, a disorder associated with aberrant expression and/or activity of integrin α.sub.Vβ.sub.3, a disorder associated with abnormal bone metabolism, a disorder associated with aberrant angiogenesis or cancer utilizing the liquid formulations of the present invention.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT pH
(5.0-7.0; anti-integrin αvβ3 antibody, fragments and formulations for treating inflammation, autoimmune disease, bone metabolic disease, angiogenesis and cancer)

IT Intestine, disease
(Crohn's; anti-integrin αvβ3 antibody, fragments and formulations for treating inflammation, autoimmune disease, bone metabolic disease, angiogenesis and cancer)

IT Angiogenic factors

IT Growth inhibitors, animal
(angiogenic growth-inhibiting factor; anti-integrin αvβ3 antibody, fragments and formulations for treating inflammation, autoimmune disease, bone metabolic disease, angiogenesis and cancer)

IT Spinal column, disease
(ankylosing spondylitis; anti-integrin αvβ3 antibody, fragments and formulations for treating inflammation, autoimmune disease, bone metabolic disease, angiogenesis and cancer)

IT Angiogenesis inhibitors

IT Anti-inflammatory agents

IT Antitumor agents
IT Arthritis
IT Autoimmune disease
IT Drug delivery systems
IT Drugs
IT Gout
IT Human
IT Immunomodulators
IT Inflammation
IT Lung, neoplasm
IT Mammary gland, neoplasm
IT Melanoma
IT Multiple sclerosis
IT Myasthenia gravis
IT Neoplasm
IT Osteoarthritis
IT Osteoporosis
IT Ovary, neoplasm
IT Physiological saline solutions
IT Prostate gland, neoplasm
IT Psoriasis
IT Rheumatoid arthritis
IT Sarcoidosis
IT Sjogren's syndrome
(anti-integrin αvβ3 antibody, fragments and formulations for treating inflammation, autoimmune disease, bone metabolic disease, angiogenesis and cancer)
IT Antibodies and Immunoglobulins
IT Oligosaccharides, biological studies
IT Polysaccharides, biological studies
(anti-integrin αvβ3 antibody, fragments and formulations for treating inflammation, autoimmune disease, bone metabolic disease, angiogenesis and cancer)
IT Standard substances, analytical
(antibody; anti-integrin αvβ3 antibody, fragments and formulations for treating inflammation, autoimmune disease, bone metabolic disease, angiogenesis and cancer)
IT Thyroid gland, disease
(autoimmune thyroiditis; anti-integrin αvβ3 antibody, fragments and formulations for treating inflammation, autoimmune disease, bone metabolic disease, angiogenesis and cancer)
IT Drug delivery systems
(carriers; anti-integrin αvβ3 antibody, fragments and formulations for treating inflammation, autoimmune disease, bone metabolic disease, angiogenesis and cancer)
IT Intestine, neoplasm
(colon; anti-integrin αvβ3 antibody, fragments and formulations for treating inflammation, autoimmune disease, bone metabolic disease, angiogenesis and cancer)
IT Medical goods
(containers; anti-integrin αvβ3 antibody, fragments and formulations for treating inflammation, autoimmune disease, bone metabolic disease, angiogenesis and cancer)
IT Joint, anatomical
(disease, degeneration; anti-integrin αvβ3 antibody, fragments and formulations for treating inflammation, autoimmune disease, bone metabolic disease, angiogenesis and cancer)
IT Joint, anatomical
(disease, neurogenic; anti-integrin αvβ3 antibody, fragments and formulations for treating inflammation, autoimmune disease, bone metabolic disease, angiogenesis and cancer)
IT Lung, disease
(fibrosis; anti-integrin αvβ3 antibody, fragments and

formulations for treating inflammation, autoimmune disease, bone metabolic disease, angiogenesis and cancer)

IT Antibodies and Immunoglobulins
(fragments; anti-integrin αvβ3 antibody, fragments and formulations for treating inflammation, autoimmune disease, bone metabolic disease, angiogenesis and cancer)

IT Surfactants
(free; anti-integrin αvβ3 antibody, fragments and formulations for treating inflammation, autoimmune disease, bone metabolic disease, angiogenesis and cancer)

IT Salts, biological studies
(free; anti-integrin αvβ3 antibody, fragments and formulations for treating inflammation, autoimmune disease, bone metabolic disease, angiogenesis and cancer)

IT Drug delivery systems
(freeze-dried; anti-integrin αvβ3 antibody, fragments and formulations for treating inflammation, autoimmune disease, bone metabolic disease, angiogenesis and cancer)

IT Neuroglia, neoplasm
(glioblastoma; anti-integrin αvβ3 antibody, fragments and formulations for treating inflammation, autoimmune disease, bone metabolic disease, angiogenesis and cancer)

IT Drug delivery systems
(injections, i.m.; anti-integrin αvβ3 antibody, fragments and formulations for treating inflammation, autoimmune disease, bone metabolic disease, angiogenesis and cancer)

IT Drug delivery systems
(injections, i.p.; anti-integrin αvβ3 antibody, fragments and formulations for treating inflammation, autoimmune disease, bone metabolic disease, angiogenesis and cancer)

IT Drug delivery systems
(injections, i.v.; anti-integrin αvβ3 antibody, fragments and formulations for treating inflammation, autoimmune disease, bone metabolic disease, angiogenesis and cancer)

IT Drug delivery systems
(injections, s.c.; anti-integrin αvβ3 antibody, fragments and formulations for treating inflammation, autoimmune disease, bone metabolic disease, angiogenesis and cancer)

IT Drug delivery systems
(injections; anti-integrin αvβ3 antibody, fragments and formulations for treating inflammation, autoimmune disease, bone metabolic disease, angiogenesis and cancer)

IT Drug delivery systems
(liqs.; anti-integrin αvβ3 antibody, fragments and formulations for treating inflammation, autoimmune disease, bone metabolic disease, angiogenesis and cancer)

IT Containers
(medical; anti-integrin αvβ3 antibody, fragments and formulations for treating inflammation, autoimmune disease, bone metabolic disease, angiogenesis and cancer)

IT Bone
(metabolism-regulating agent; anti-integrin αvβ3 antibody, fragments and formulations for treating inflammation, autoimmune disease, bone metabolic disease, angiogenesis and cancer)

IT Bone, neoplasm
(metastasis; anti-integrin αvβ3 antibody, fragments and formulations for treating inflammation, autoimmune disease, bone metabolic disease, angiogenesis and cancer)

IT Drug delivery systems
(nasal, intra-; anti-integrin αvβ3 antibody, fragments and formulations for treating inflammation, autoimmune disease, bone metabolic disease, angiogenesis and cancer)

IT Drug delivery systems

(oral; anti-integrin αvβ3 antibody, fragments and formulations for treating inflammation, autoimmune disease, bone metabolic disease, angiogenesis and cancer)

IT Bone, disease
(osteolysis, inflammatory; anti-integrin αvβ3 antibody, fragments and formulations for treating inflammation, autoimmune disease, bone metabolic disease, angiogenesis and cancer)

IT Bone, disease
(osteopenia; anti-integrin αvβ3 antibody, fragments and formulations for treating inflammation, autoimmune disease, bone metabolic disease, angiogenesis and cancer)

IT Drug delivery systems
(parenterals; anti-integrin αvβ3 antibody, fragments and formulations for treating inflammation, autoimmune disease, bone metabolic disease, angiogenesis and cancer)

IT Skin, disease
(pemphigus vulgaris; anti-integrin αvβ3 antibody, fragments and formulations for treating inflammation, autoimmune disease, bone metabolic disease, angiogenesis and cancer)

IT Arthritis
(peri-; scapulohumeral; anti-integrin αvβ3 antibody, fragments and formulations for treating inflammation, autoimmune disease, bone metabolic disease, angiogenesis and cancer)

IT Alcohols, biological studies
(polyhydric; anti-integrin αvβ3 antibody, fragments and formulations for treating inflammation, autoimmune disease, bone metabolic disease, angiogenesis and cancer)

IT Muscle, disease
(polymyositis; anti-integrin αvβ3 antibody, fragments and formulations for treating inflammation, autoimmune disease, bone metabolic disease, angiogenesis and cancer)

IT Arthritis
(pseudogout; anti-integrin αvβ3 antibody, fragments and formulations for treating inflammation, autoimmune disease, bone metabolic disease, angiogenesis and cancer)

IT Arthritis
(psoriatic arthritis; anti-integrin αvβ3 antibody, fragments and formulations for treating inflammation, autoimmune disease, bone metabolic disease, angiogenesis and cancer)

IT Connective tissue, disease
(scleroderma; anti-integrin αvβ3 antibody, fragments and formulations for treating inflammation, autoimmune disease, bone metabolic disease, angiogenesis and cancer)

IT High-performance gel-permeation chromatography
(size-exclusion; HPSEC; anti-integrin αvβ3 antibody, fragments and formulations for treating inflammation, autoimmune disease, bone metabolic disease, angiogenesis and cancer)

IT Lupus erythematosus
(systemic; anti-integrin αvβ3 antibody, fragments and formulations for treating inflammation, autoimmune disease, bone metabolic disease, angiogenesis and cancer)

IT Intestine, disease
(ulcerative colitis; anti-integrin αvβ3 antibody, fragments and formulations for treating inflammation, autoimmune disease, bone metabolic disease, angiogenesis and cancer)

IT Blood vessel, disease
(vasculitis; anti-integrin αvβ3 antibody, fragments and formulations for treating inflammation, autoimmune disease, bone metabolic disease, angiogenesis and cancer)

IT Integrins
(αvβ3; anti-integrin αvβ3 antibody, fragments and formulations for treating inflammation, autoimmune disease, bone metabolic disease, angiogenesis and cancer)

IT 71-00-1, L-Histidine, biological studies 7732-18-5, Water, biological studies 303127-73-3, MEDI-522
(anti-integrin αvβ3 antibody, fragments and formulations for treating inflammation, autoimmune disease, bone metabolic disease, angiogenesis and cancer)
IT 162290-66-6 211373-80-7 315667-90-4 315667-92-6 459123-09-2 459123-10-5
(unclaimed sequence; anti-integrin αvβ3 antibody, fragments and formulations for treating inflammation, autoimmune disease, bone metabolic disease, angiogenesis and cancer)

L15 ANSWER 49 OF 55 USPATFULL on STN
ACCESSION NUMBER: 2004:267332 USPATFULL
TITLE: Uses of anti-integrin alphanubeta3 antibody formulations
INVENTOR(S): Allan, Christian B., Brookeville, MD, UNITED STATES
PATENT ASSIGNEE(S): MedImmune, Inc. (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2004208869	A1	20041021
APPLICATION INFO.:	US 2004-769700	A1	20040130 (10)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2003-443810P	20030130 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: JONES DAY, 222 EAST 41ST ST, NEW YORK, NY, 10017
NUMBER OF CLAIMS: 40
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 1 Drawing Page(s)
LINE COUNT: 6223
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention provides liquid formulations of antibodies or antibody fragments that immunospecifically bind to integrin α.sub.vβ.sub.3, which formulations exhibit stability, low to undetectable levels of aggregation, and very little to no loss of the biological activities of the antibodies or antibody fragments, even during long periods of storage. In particular, the present invention provides liquid formulations of antibodies or fragments thereof that immunospecifically bind to integrin α.sub.vβ.sub.3, which formulations are substantially free of surfactant, inorganic salts, and/or other common excipients. Furthermore, the invention provides methods of preventing, treating or ameliorating an inflammatory disorder, an autoimmune disorder, a disorder associated with aberrant expression and/or activity of integrin α.sub.vβ.sub.3, a disorder associated with abnormal bone metabolism, a disorder associated with aberrant angiogenesis or cancer utilizing the liquid formulations of the present invention.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT pH
(5.0-7.0; anti-integrin αvβ3 antibody, fragments and formulations for treating inflammation, autoimmune disease, bone metabolic disease, angiogenesis and cancer)
IT Intestine, disease
(Crohn's; anti-integrin αvβ3 antibody, fragments and formulations for treating inflammation, autoimmune disease, bone metabolic disease, angiogenesis and cancer)
IT Angiogenic factors
IT Growth inhibitors, animal
(angiogenic growth-inhibiting factor; anti-integrin αvβ3

antibody, fragments and formulations for treating inflammation, autoimmune disease, bone metabolic disease, angiogenesis and cancer)

IT Spinal column, disease
(ankylosing spondylitis; anti-integrin αvβ3 antibody, fragments and formulations for treating inflammation, autoimmune disease, bone metabolic disease, angiogenesis and cancer)

IT Angiogenesis inhibitors
IT Anti-inflammatory agents
IT Antitumor agents
IT Arthritis
IT Autoimmune disease
IT Drug delivery systems
IT Drugs
IT Gout
IT Human
IT Immunomodulators
IT Inflammation
IT Lung, neoplasm
IT Mammary gland, neoplasm
IT Melanoma
IT Multiple sclerosis
IT Myasthenia gravis
IT Neoplasm
IT Osteoarthritis
IT Osteoporosis
IT Ovary, neoplasm
IT Physiological saline solutions
IT Prostate gland, neoplasm
IT Psoriasis
IT Rheumatoid arthritis
IT Sarcoidosis
IT Sjogren's syndrome
(anti-integrin αvβ3 antibody, fragments and formulations for treating inflammation, autoimmune disease, bone metabolic disease, angiogenesis and cancer)

IT Antibodies and Immunoglobulins
IT Oligosaccharides, biological studies
IT Polysaccharides, biological studies
(anti-integrin αvβ3 antibody, fragments and formulations for treating inflammation, autoimmune disease, bone metabolic disease, angiogenesis and cancer)

IT Standard substances, analytical
(antibody; anti-integrin αvβ3 antibody, fragments and formulations for treating inflammation, autoimmune disease, bone metabolic disease, angiogenesis and cancer)

IT Thyroid gland, disease
(autoimmune thyroiditis; anti-integrin αvβ3 antibody, fragments and formulations for treating inflammation, autoimmune disease, bone metabolic disease, angiogenesis and cancer)

IT Drug delivery systems
(carriers; anti-integrin αvβ3 antibody, fragments and formulations for treating inflammation, autoimmune disease, bone metabolic disease, angiogenesis and cancer)

IT Intestine, neoplasm
(colon; anti-integrin αvβ3 antibody, fragments and formulations for treating inflammation, autoimmune disease, bone metabolic disease, angiogenesis and cancer)

IT Medical goods
(containers; anti-integrin αvβ3 antibody, fragments and formulations for treating inflammation, autoimmune disease, bone metabolic disease, angiogenesis and cancer)

IT Joint, anatomical
(disease, degeneration; anti-integrin αvβ3 antibody,

fragments and formulations for treating inflammation, autoimmune disease, bone metabolic disease, angiogenesis and cancer)

IT Joint, anatomical
(disease, neurogenic; anti-integrin αvβ3 antibody, fragments and formulations for treating inflammation, autoimmune disease, bone metabolic disease, angiogenesis and cancer)

IT Lung, disease
(fibrosis; anti-integrin αvβ3 antibody, fragments and formulations for treating inflammation, autoimmune disease, bone metabolic disease, angiogenesis and cancer)

IT Antibodies and Immunoglobulins
(fragments; anti-integrin αvβ3 antibody, fragments and formulations for treating inflammation, autoimmune disease, bone metabolic disease, angiogenesis and cancer)

IT Surfactants
(free; anti-integrin αvβ3 antibody, fragments and formulations for treating inflammation, autoimmune disease, bone metabolic disease, angiogenesis and cancer)

IT Salts, biological studies
(free; anti-integrin αvβ3 antibody, fragments and formulations for treating inflammation, autoimmune disease, bone metabolic disease, angiogenesis and cancer)

IT Drug delivery systems
(freeze-dried; anti-integrin αvβ3 antibody, fragments and formulations for treating inflammation, autoimmune disease, bone metabolic disease, angiogenesis and cancer)

IT Neuroglia, neoplasm
(glioblastoma; anti-integrin αvβ3 antibody, fragments and formulations for treating inflammation, autoimmune disease, bone metabolic disease, angiogenesis and cancer)

IT Drug delivery systems
(injections, i.m.; anti-integrin αvβ3 antibody, fragments and formulations for treating inflammation, autoimmune disease, bone metabolic disease, angiogenesis and cancer)

IT Drug delivery systems
(injections, i.p.; anti-integrin αvβ3 antibody, fragments and formulations for treating inflammation, autoimmune disease, bone metabolic disease, angiogenesis and cancer)

IT Drug delivery systems
(injections, i.v.; anti-integrin αvβ3 antibody, fragments and formulations for treating inflammation, autoimmune disease, bone metabolic disease, angiogenesis and cancer)

IT Drug delivery systems
(injections, s.c.; anti-integrin αvβ3 antibody, fragments and formulations for treating inflammation, autoimmune disease, bone metabolic disease, angiogenesis and cancer)

IT Drug delivery systems
(injections; anti-integrin αvβ3 antibody, fragments and formulations for treating inflammation, autoimmune disease, bone metabolic disease, angiogenesis and cancer)

IT Drug delivery systems
(liqs.; anti-integrin αvβ3 antibody, fragments and formulations for treating inflammation, autoimmune disease, bone metabolic disease, angiogenesis and cancer)

IT Containers
(medical; anti-integrin αvβ3 antibody, fragments and formulations for treating inflammation, autoimmune disease, bone metabolic disease, angiogenesis and cancer)

IT Bone
(metabolism-regulating agent; anti-integrin αvβ3 antibody, fragments and formulations for treating inflammation, autoimmune disease, bone metabolic disease, angiogenesis and cancer)

IT Bone, neoplasm

(metastasis; anti-integrin αvβ3 antibody, fragments and formulations for treating inflammation, autoimmune disease, bone metabolic disease, angiogenesis and cancer)

IT Drug delivery systems
(nasal, intra-; anti-integrin αvβ3 antibody, fragments and formulations for treating inflammation, autoimmune disease, bone metabolic disease, angiogenesis and cancer)

IT Drug delivery systems
(oral; anti-integrin αvβ3 antibody, fragments and formulations for treating inflammation, autoimmune disease, bone metabolic disease, angiogenesis and cancer)

IT Bone, disease
(osteolysis, inflammatory; anti-integrin αvβ3 antibody, fragments and formulations for treating inflammation, autoimmune disease, bone metabolic disease, angiogenesis and cancer)

IT Bone, disease
(osteopenia; anti-integrin αvβ3 antibody, fragments and formulations for treating inflammation, autoimmune disease, bone metabolic disease, angiogenesis and cancer)

IT Drug delivery systems
(parenterals; anti-integrin αvβ3 antibody, fragments and formulations for treating inflammation, autoimmune disease, bone metabolic disease, angiogenesis and cancer)

IT Skin, disease
(pemphigus vulgaris; anti-integrin αvβ3 antibody, fragments and formulations for treating inflammation, autoimmune disease, bone metabolic disease, angiogenesis and cancer)

IT Arthritis
(peri-; scapulohumeral; anti-integrin αvβ3 antibody, fragments and formulations for treating inflammation, autoimmune disease, bone metabolic disease, angiogenesis and cancer)

IT Alcohols, biological studies
(polyhydric; anti-integrin αvβ3 antibody, fragments and formulations for treating inflammation, autoimmune disease, bone metabolic disease, angiogenesis and cancer)

IT Muscle, disease
(polymyositis; anti-integrin αvβ3 antibody, fragments and formulations for treating inflammation, autoimmune disease, bone metabolic disease, angiogenesis and cancer)

IT Arthritis
(pseudogout; anti-integrin αvβ3 antibody, fragments and formulations for treating inflammation, autoimmune disease, bone metabolic disease, angiogenesis and cancer)

IT Arthritis
(psoriatic arthritis; anti-integrin αvβ3 antibody, fragments and formulations for treating inflammation, autoimmune disease, bone metabolic disease, angiogenesis and cancer)

IT Connective tissue, disease
(scleroderma; anti-integrin αvβ3 antibody, fragments and formulations for treating inflammation, autoimmune disease, bone metabolic disease, angiogenesis and cancer)

IT High-performance gel-permeation chromatography
(size-exclusion; HPSEC; anti-integrin αvβ3 antibody, fragments and formulations for treating inflammation, autoimmune disease, bone metabolic disease, angiogenesis and cancer)

IT Lupus erythematosus
(systemic; anti-integrin αvβ3 antibody, fragments and formulations for treating inflammation, autoimmune disease, bone metabolic disease, angiogenesis and cancer)

IT Intestine, disease
(ulcerative colitis; anti-integrin αvβ3 antibody, fragments and formulations for treating inflammation, autoimmune disease, bone metabolic disease, angiogenesis and cancer)

IT Blood vessel, disease
(vasculitis; anti-integrin αvβ3 antibody, fragments and formulations for treating inflammation, autoimmune disease, bone metabolic disease, angiogenesis and cancer)
IT Integrins
(αvβ3; anti-integrin αvβ3 antibody, fragments and formulations for treating inflammation, autoimmune disease, bone metabolic disease, angiogenesis and cancer)
IT 71-00-1, L-Histidine, biological studies 7732-18-5, Water, biological studies 303127-73-3, MEDI-522
(anti-integrin αvβ3 antibody, fragments and formulations for treating inflammation, autoimmune disease, bone metabolic disease, angiogenesis and cancer)
IT 162290-66-6 211373-80-7 315667-90-4 315667-92-6 459123-09-2 459123-10-5
(unclaimed sequence; anti-integrin αvβ3 antibody, fragments and formulations for treating inflammation, autoimmune disease, bone metabolic disease, angiogenesis and cancer)

L15 ANSWER 50 OF 55 USPATFULL on STN
ACCESSION NUMBER: 2006:216869 USPATFULL
TITLE: Systems and methods for identifying miRNA targets and for altering miRNA and target expression
INVENTOR(S): Bartel, David, Brookline, MA, UNITED STATES
Lewis, Benjamin P., Cambridge, MA, UNITED STATES
Jones-Rhoades, Matthew W., Somerville, MA, UNITED STATES
Burge, Christopher B., Belmont, MA, UNITED STATES

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2006185027	A1	20060817	
APPLICATION INFO.:	US 2005-317660	A1	20051223	(11)

	NUMBER	DATE	
PRIORITY INFORMATION:	US 2004-639231P	20041223	(60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: WOLF GREENFIELD & SACKS, PC, FEDERAL RESERVE PLAZA, 600 ATLANTIC AVENUE, BOSTON, MA, 02210-2206, US
NUMBER OF CLAIMS: 28
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 46 Drawing Page(s)
LINE COUNT: 12767
AB The present invention generally relates to microRNAs such as vertebrate microRNA (miRNA), for example, mammalian miRNA. Various aspects of the invention are directed to the detection, production, or expression of miRNA. In one aspect, the invention provides systems and methods for identifying targets of miRNA sequences. For instance, in one embodiment, gene sequences comprising UTRs are compared with miRNA sequences to determine the degree of interaction, for example, by determining a free energy measurement between the miRNA sequence and the UTR, and/or by determining complementarity between at least a portion of the miRNA sequence and the UTR. In another aspect, the invention is directed to the regulation of gene expression using miRNA. For example, gene expression within a cell may be altered by exposing the cell to an oligonucleotide comprising a sequence that is substantially antisense to at least a portion of an miRNA region of the gene, for example, antisense to a 6-mer or 7-mer portion of the miRNA. In still another aspect, the invention is directed to the treatment of cancer. For instance, in one set of embodiments, an isolated oligonucleotide comprising a sequence that is substantially antisense to an miRNA, or a

portion of an miRNA, is administered to a subject having or being at risk of cancer. Yet other aspects of the invention are directed to compositions or kits including oligonucleotides comprising a sequence that is substantially antisense to an miRNA (or a portion of an miRNA), methods of promoting any of the above aspects, or the like.

L15 ANSWER 51 OF 55 USPATFULL on STN

ACCESSION NUMBER:	2004:1816 USPATFULL
TITLE:	Prevention or treatment of cancer using integrin alphavbeta3 antagonists in combination with other agents
INVENTOR(S):	Woessner, Richard, Lafayette, CO, UNITED STATES Kiener, Peter, Doylestwon, PA, UNITED STATES Dormitzer, Melissa, Germantown, MD, UNITED STATES Walsh, William, Sharpsburg, MD, UNITED STATES Heinrichs, Jon, North Potomac, MD, UNITED STATES
PATENT ASSIGNEE(S):	MedImmune, Inc. (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2004001835	A1	20040101	
APPLICATION INFO.:	US 2003-379189	A1	20030304	(10)

	NUMBER	DATE	
PRIORITY INFORMATION:	US 2002-361859P	20020304	(60)
	US 2002-370398P	20020405	(60)
	US 2003-444265P	20030130	(60)

DOCUMENT TYPE:	Utility
FILE SEGMENT:	APPLICATION
LEGAL REPRESENTATIVE:	PENNIE AND EDMONDS, 1155 AVENUE OF THE AMERICAS, NEW YORK, NY, 100362711
NUMBER OF CLAIMS:	44
EXEMPLARY CLAIM:	1
NUMBER OF DRAWINGS:	8 Drawing Page(s)
LINE COUNT:	6588

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates to methods and compositions designed for the treatment, management or prevention of cancer. The methods of the invention comprise the administration of an effective amount of one or more antagonists of Integrin α.sub.Vβ.sub.3 alone or in combination with the administration of an effective amount of one or more other agents useful for cancer therapy. The invention also provides pharmaceutical compositions comprising one or more antagonists of Integrin α.sub.Vβ.sub.3 and/or one or more other agents useful for cancer therapy. In particular, the invention is directed to methods of treatment and prevention of cancer by the administration of a therapeutically or prophylactically effective amount of one or more antagonists of Integrin α.sub.Vβ.sub.3 alone or in combination with standard and experimental therapies for treatment or prevention of cancer. Also included are methods for screening for epitope-specific Integrin α.sub.Vβ.sub.3 antagonists which can be used according to the methods of the invention. In addition, methods for facilitating the use of Integrin α.sub.Vβ.sub.3 antagonists in the analysis of Integrin α.sub.Vβ.sub.3 expression in biopsies of animal model and clinical study samples are also contemplated.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT Intestine, disease
(Crohn's; preventing or treating disorders by administering an integrin αvβ3 antagonist in combination with an HMG-CoA reductase

inhibitor or a bisphosphonate or other therapeutic agent)

IT Bone, disease
(Gorham-Stout disease; preventing or treating disorders by administering an integrin αvβ3 antagonist in combination with an HMG-CoA reductase inhibitor or a bisphosphonate or other therapeutic agent)

IT Bone, disease
(Paget's; preventing or treating disorders by administering an integrin αvβ3 antagonist in combination with an HMG-CoA reductase inhibitor or a bisphosphonate or other therapeutic agent)

IT Angiogenesis
(aberrant; preventing or treating disorders by administering an integrin αvβ3 antagonist in combination with an HMG-CoA reductase inhibitor or a bisphosphonate or other therapeutic agent)

IT Antibodies
(anti-integrin αvβ3; preventing or treating disorders by administering an integrin αvβ3 antagonist in combination with an HMG-CoA reductase inhibitor or a bisphosphonate or other therapeutic agent)

IT Antiarteriosclerotics
(antiatherosclerotics; preventing or treating disorders by administering an integrin αvβ3 antagonist in combination with an HMG-CoA reductase inhibitor or a bisphosphonate or other therapeutic agent)

IT Intestine, neoplasm
(colon; preventing or treating disorders by administering an integrin αvβ3 antagonist in combination with an HMG-CoA reductase inhibitor or a bisphosphonate or other therapeutic agent)

IT Eye, disease
(diabetic retinopathy; preventing or treating disorders by administering an integrin αvβ3 antagonist in combination with an HMG-CoA reductase inhibitor or a bisphosphonate or other therapeutic agent)

IT Joint, anatomical
(disease, aseptic loosening of replacement; preventing or treating disorders by administering an integrin αvβ3 antagonist in combination with an HMG-CoA reductase inhibitor or a bisphosphonate or other therapeutic agent)

IT Eye, disease
(macula, degeneration; preventing or treating disorders by administering an integrin αvβ3 antagonist in combination with an HMG-CoA reductase inhibitor or a bisphosphonate or other therapeutic agent)

IT Bone, neoplasm
(metastasis; preventing or treating disorders by administering an integrin αvβ3 antagonist in combination with an HMG-CoA reductase inhibitor or a bisphosphonate or other therapeutic agent)

IT Estrogen receptors
(modulators; preventing or treating disorders by administering an integrin αvβ3 antagonist in combination with an HMG-CoA reductase inhibitor or a bisphosphonate or other therapeutic agent)

IT Bone, disease
(osteolysis, inflammatory; preventing or treating disorders by administering an integrin αvβ3 antagonist in combination with an HMG-CoA reductase inhibitor or a bisphosphonate or other therapeutic agent)

IT Bone, disease
(osteopenia; preventing or treating disorders by administering an integrin αvβ3 antagonist in combination with an HMG-CoA reductase inhibitor or a bisphosphonate or other therapeutic agent)

IT Angiogenesis inhibitors

IT Anti-inflammatory agents

IT Antiarthritics

IT Antirheumatic agents
IT Antitumor agents
IT Arthritis
IT Atherosclerosis
IT Autoimmune disease
IT Behcet's syndrome
IT Bone, neoplasm
IT Drug interactions
IT Human
IT Immunomodulators
IT Inflammation
IT Lung, neoplasm
IT Mammary gland, neoplasm
IT Melanoma
IT Neoplasm
IT Osteoarthritis
IT Osteoporosis
IT Ovary, neoplasm
IT Periodontium, disease
IT Prostate gland, neoplasm
IT Radiotherapy
IT Rheumatoid arthritis
(preventing or treating disorders by administering an integrin αvβ3 antagonist in combination with an HMG-CoA reductase inhibitor or a bisphosphonate or other therapeutic agent)
IT Estrogens
(preventing or treating disorders by administering an integrin αvβ3 antagonist in combination with an HMG-CoA reductase inhibitor or a bisphosphonate or other therapeutic agent)
IT Artery, disease
(restenosis; preventing or treating disorders by administering an integrin αvβ3 antagonist in combination with an HMG-CoA reductase inhibitor or a bisphosphonate or other therapeutic agent)
IT Integrins
(αvβ3; preventing or treating disorders by administering an integrin αvβ3 antagonist in combination with an HMG-CoA reductase inhibitor or a bisphosphonate or other therapeutic agent)
IT 9028-35-7, 3-Hydroxy-3-methylglutaryl CoA reductase
(HMG-CoA reductase; preventing or treating disorders by administering an integrin αvβ3 antagonist in combination with an HMG-CoA reductase inhibitor or a bisphosphonate or other therapeutic agent)
IT 153377-38-9, GenBank L28832
(methods of preventing or treating disorders by administering an integrin αvβ3 antagonist in combination with an HMG-CoA reductase inhibitor or a bisphosphonate)
IT 1406-16-2, Vitamin D 9007-12-9, Calcitonin 13598-36-2D, Phosphonic acid, alkylidenebis- derivs. 324740-00-3, VITAXIN
(preventing or treating disorders by administering an integrin αvβ3 antagonist in combination with an HMG-CoA reductase inhibitor or a bisphosphonate or other therapeutic agent)
IT 162290-66-6 211373-80-7 315667-90-4 315667-92-6 459123-09-2 459123-10-5
(unclaimed sequence; methods of preventing or treating disorders by administering an integrin αvβ3 antagonist in combination with an HMG-CoA reductase inhibitor or a bisphosphonate)

L15 ANSWER 52 OF 55 USPATFULL on STN
ACCESSION NUMBER: 2006:143528 USPATFULL
TITLE: Modulation of antibody specificity by tailoring the affinity to cognate antigens
INVENTOR(S): Dall'Acqua, William, Gaithersburg, MD, UNITED STATES
Damschroder, Melissa, Germantown, MD, UNITED STATES
Kinch, Michael S., Laytonsville, MD, UNITED STATES

	Carles-Kinch, Kelly, Laytonsville, MD, UNITED STATES
PATENT ASSIGNEE(S):	MEDIMMUNE, INC., Gaithersburg, MD, UNITED STATES (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2006121042	A1	20060608	
APPLICATION INFO.:	US 2005-259133	A1	20051027	(11)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2004-622711P	20041027 (60)
	US 2005-717209P	20050916 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: JONATHAN KLEIN-EVANS, ONE MEDIMMUNE WAY, GAITHERSBURG, MD, 20878, US
NUMBER OF CLAIMS: 64
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 62 Drawing Page(s)
LINE COUNT: 12411
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates to methods and compositions designed for the treatment, management, prevention and/or amelioration of various disorders associated with aberrant expression and/or activity of one or more Eph receptor tyrosine kinase family members and/or one or more Eph receptor ligands, particularly the Ephrins. In particular, the invention provides methods for the treatment, management, prevention and/or amelioration of a disorder associated with aberrant expression and/or activity(ies) of one or more Eph receptors and/or one or more Ephrins; the method comprising administering to a subject in need thereof an effective amount of one or more Eph/Ephrin Modulators. The present invention further relates to methods of modulating antibody specificity by tailoring the affinity to cognate antigens.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT EphA receptors
(10; affinity-optimized combinatorial variants of antibody specific to Eph receptor and/or Ephrin for treating cancer and inflammation)
IT EphB receptors
(5; affinity-optimized combinatorial variants of antibody specific to Eph receptor and/or Ephrin for treating cancer and inflammation)
IT EphA receptors
(6; affinity-optimized combinatorial variants of antibody specific to Eph receptor and/or Ephrin for treating cancer and inflammation)
IT Ephrins
(A1; affinity-optimized combinatorial variants of antibody specific to Eph receptor and/or Ephrin for treating cancer and inflammation)
IT Ephrins
(A4; affinity-optimized combinatorial variants of antibody specific to Eph receptor and/or Ephrin for treating cancer and inflammation)
IT Ephrins
(B1; affinity-optimized combinatorial variants of antibody specific to Eph receptor and/or Ephrin for treating cancer and inflammation)
IT Inflammation
(Crohn's disease; affinity-optimized combinatorial variants of antibody specific to Eph receptor and/or Ephrin for treating cancer and inflammation)
IT Intestine, disease
(Crohn's; affinity-optimized combinatorial variants of antibody specific to Eph receptor and/or Ephrin for treating cancer and inflammation)
IT Ligands

(Eph receptor; affinity-optimized combinatorial variants of antibody specific to Eph receptor and/or Ephrin for treating cancer and inflammation)

IT Antisense nucleic acids
(Eph receptor; affinity-optimized combinatorial variants of antibody specific to Eph receptor and/or Ephrin for treating cancer and inflammation)

IT Ribozymes
(Eph receptor; affinity-optimized combinatorial variants of antibody specific to Eph receptor and/or Ephrin for treating cancer and inflammation)

IT EphA receptors
(EphA1; affinity-optimized combinatorial variants of antibody specific to Eph receptor and/or Ephrin for treating cancer and inflammation)

IT EphA receptors
(EphA4; affinity-optimized combinatorial variants of antibody specific to Eph receptor and/or Ephrin for treating cancer and inflammation)

IT EphA receptors
(EphA5; affinity-optimized combinatorial variants of antibody specific to Eph receptor and/or Ephrin for treating cancer and inflammation)

IT EphA receptors
(EphA7; affinity-optimized combinatorial variants of antibody specific to Eph receptor and/or Ephrin for treating cancer and inflammation)

IT EphA receptors
(EphA8; affinity-optimized combinatorial variants of antibody specific to Eph receptor and/or Ephrin for treating cancer and inflammation)

IT EphB receptors
(EphB1; affinity-optimized combinatorial variants of antibody specific to Eph receptor and/or Ephrin for treating cancer and inflammation)

IT EphB receptors
(EphB2; affinity-optimized combinatorial variants of antibody specific to Eph receptor and/or Ephrin for treating cancer and inflammation)

IT EphB receptors
(EphB3; affinity-optimized combinatorial variants of antibody specific to Eph receptor and/or Ephrin for treating cancer and inflammation)

IT EphB receptors
(EphB4; affinity-optimized combinatorial variants of antibody specific to Eph receptor and/or Ephrin for treating cancer and inflammation)

IT EphB receptors
(EphB6; affinity-optimized combinatorial variants of antibody specific to Eph receptor and/or Ephrin for treating cancer and inflammation)

IT Antibodies and Immunoglobulins
(IgG1; affinity-optimized combinatorial variants of antibody specific to Eph receptor and/or Ephrin for treating cancer and inflammation)

IT Disease, animal
(PLCH; affinity-optimized combinatorial variants of antibody specific to Eph receptor and/or Ephrin for treating cancer and inflammation)

IT Adoptive immunotherapy

IT Alzheimer's disease

IT Animal cell line

IT Antitumor agents

IT Bone, neoplasm

IT Cirrhosis

IT Combinatorial library

IT Epitopes

IT Esophagus, neoplasm

IT Human

IT Inflammation

IT Kidney, neoplasm

IT Liver, neoplasm

IT Lung, neoplasm

IT Mammary gland, neoplasm

IT Neoplasm

IT Ovary, neoplasm
IT Pancreas, neoplasm
IT Phage display library
IT Prophylaxis
IT Prostate gland, neoplasm
IT Protein sequences
IT Psoriasis
IT Skin, neoplasm
IT Stomach, neoplasm
IT Testis, neoplasm
IT Thyroid gland, neoplasm
IT Uterus, neoplasm
IT cDNA sequences
(affinity-optimized combinatorial variants of antibody specific to Eph receptor and/or Ephrin for treating cancer and inflammation)
IT Fusion proteins (chimeric proteins)
(affinity-optimized combinatorial variants of antibody specific to Eph receptor and/or Ephrin for treating cancer and inflammation)
IT Antibodies and Immunoglobulins
(affinity-optimized combinatorial variants of antibody specific to Eph receptor and/or Ephrin for treating cancer and inflammation)
IT Eph receptors
IT Ephrin-A2
IT Ephrin-A3
IT Ephrin-A5
IT Ephrin-B2
IT Ephrin-B3
IT Ephrins
(affinity-optimized combinatorial variants of antibody specific to Eph receptor and/or Ephrin for treating cancer and inflammation)
IT Autoimmune disease
IT Inflammation
IT Thyroid gland, disease
(autoimmune thyroiditis; affinity-optimized combinatorial variants of antibody specific to Eph receptor and/or Ephrin for treating cancer and inflammation)
IT Cell migration
IT Molecular cloning
(cancer cell inhibition; affinity-optimized combinatorial variants of antibody specific to Eph receptor and/or Ephrin for treating cancer and inflammation)
IT Synovial fluid
(cancer; affinity-optimized combinatorial variants of antibody specific to Eph receptor and/or Ephrin for treating cancer and inflammation)
IT Inflammation
(carditis, granulomatous; affinity-optimized combinatorial variants of antibody specific to Eph receptor and/or Ephrin for treating cancer and inflammation)
IT Uterus, neoplasm
(cervix; affinity-optimized combinatorial variants of antibody specific to Eph receptor and/or Ephrin for treating cancer and inflammation)
IT Antibodies and Immunoglobulins
(chimeric; affinity-optimized combinatorial variants of antibody specific to Eph receptor and/or Ephrin for treating cancer and inflammation)
IT Gallbladder, disease
IT Inflammation
(cholecystitis, acute; affinity-optimized combinatorial variants of antibody specific to Eph receptor and/or Ephrin for treating cancer and inflammation)
IT Inflammation
IT Pancreas, disease
(chronic pancreatitis; affinity-optimized combinatorial variants of

antibody specific to Eph receptor and/or Ephrin for treating cancer and inflammation)

IT Intestine, neoplasm
(colon; affinity-optimized combinatorial variants of antibody specific to Eph receptor and/or Ephrin for treating cancer and inflammation)

IT Heart, disease
(dilated cardiomyopathy, primary congestive; affinity-optimized combinatorial variants of antibody specific to Eph receptor and/or Ephrin for treating cancer and inflammation)

IT Heart, disease
(dilated cardiomyopathy, primary dilated; affinity-optimized combinatorial variants of antibody specific to Eph receptor and/or Ephrin for treating cancer and inflammation)

IT Inflammation

IT Intestine, disease
(diverticulitis; affinity-optimized combinatorial variants of antibody specific to Eph receptor and/or Ephrin for treating cancer and inflammation)

IT Uterus, neoplasm
(endometrium; affinity-optimized combinatorial variants of antibody specific to Eph receptor and/or Ephrin for treating cancer and inflammation)

IT Tyrosine kinase receptors
(ephrin type-A receptor 2; affinity-optimized combinatorial variants of antibody specific to Eph receptor and/or Ephrin for treating cancer and inflammation)

IT Tyrosine kinase receptors
(ephrin type-A receptor 3; affinity-optimized combinatorial variants of antibody specific to Eph receptor and/or Ephrin for treating cancer and inflammation)

IT Antibodies and Immunoglobulins
(fragments, Fc; affinity-optimized combinatorial variants of antibody specific to Eph receptor and/or Ephrin for treating cancer and inflammation)

IT Transplant and Transplantation
(graft-vs.-host reaction; affinity-optimized combinatorial variants of antibody specific to Eph receptor and/or Ephrin for treating cancer and inflammation)

IT Antibodies and Immunoglobulins
(heavy chain, V region; affinity-optimized combinatorial variants of antibody specific to Eph receptor and/or Ephrin for treating cancer and inflammation)

IT Antibodies and Immunoglobulins
(humanized; affinity-optimized combinatorial variants of antibody specific to Eph receptor and/or Ephrin for treating cancer and inflammation)

IT Eukaryota

IT Prokaryota
(library; affinity-optimized combinatorial variants of antibody specific to Eph receptor and/or Ephrin for treating cancer and inflammation)

IT Antibodies and Immunoglobulins
(light chain, V region; affinity-optimized combinatorial variants of antibody specific to Eph receptor and/or Ephrin for treating cancer and inflammation)

IT Neoplasm
(metastasis, inhibition; affinity-optimized combinatorial variants of antibody specific to Eph receptor and/or Ephrin for treating cancer and inflammation)

IT Antibodies and Immunoglobulins
(monoclonal; affinity-optimized combinatorial variants of antibody specific to Eph receptor and/or Ephrin for treating cancer and inflammation)

IT Heart, disease
IT Inflammation
(myocarditis, granulomatous; affinity-optimized combinatorial variants of antibody specific to Eph receptor and/or Ephrin for treating cancer and inflammation)
IT Affinity
(optimization; affinity-optimized combinatorial variants of antibody specific to Eph receptor and/or Ephrin for treating cancer and inflammation)
IT Salivary gland
(parotid, cancer; affinity-optimized combinatorial variants of antibody specific to Eph receptor and/or Ephrin for treating cancer and inflammation)
IT Intestine, neoplasm
(rectum; affinity-optimized combinatorial variants of antibody specific to Eph receptor and/or Ephrin for treating cancer and inflammation)
IT Double stranded RNA
(small interfering, Eph receptor; affinity-optimized combinatorial variants of antibody specific to Eph receptor and/or Ephrin for treating cancer and inflammation)
IT Animal tissue, disease
(soft, neoplasm; affinity-optimized combinatorial variants of antibody specific to Eph receptor and/or Ephrin for treating cancer and inflammation)
IT Neoplasm
(soft-tissue; affinity-optimized combinatorial variants of antibody specific to Eph receptor and/or Ephrin for treating cancer and inflammation)
IT Inflammation
IT Intestine, disease
(ulcerative colitis; affinity-optimized combinatorial variants of antibody specific to Eph receptor and/or Ephrin for treating cancer and inflammation)
IT 885234-71-9P 885234-72-0P 885234-73-1P 885234-74-2P 885234-75-3P
885234-76-4P 885234-77-5P 885234-78-6P 885234-79-7P 885234-80-0P
885234-81-1P 885234-82-2P 885234-83-3P 885234-84-4P 885234-85-5P
885234-86-6P 885234-87-7P
(amino acid sequence; affinity-optimized combinatorial variants of antibody specific to Eph receptor and/or Ephrin for treating cancer and inflammation)
IT 813408-65-0, GenBank CAI43321 885234-16-2 885234-18-4 885234-20-8
885234-22-0 885234-24-2 885234-26-4 885234-28-6 885234-30-0
885234-32-2 885234-34-4 885234-36-6 885234-38-8 885234-40-2
885234-42-4 885234-45-7 885234-46-8 885234-48-0, Ephrin A1 (Human variant 1) 885234-50-4, Ephrin A1 (Human variant 2) 885234-52-6, Ephrin A2 (Human) 885234-54-8, Ephrin A3 (Human) 885234-56-0, Ephrin A4 (Human variant 1) 885234-58-2, Ephrin A4 (Human variant 2) 885234-60-6, Ephrin A4 (Human variant 3) 885234-62-8, Ephrin A5 (Human)
885234-64-0, Ephrin B1 (Human) 885234-66-2, Ephrin B2 (Human)
885234-68-4, Ephrin B3 (Human) 885234-70-8
(amino acid sequence; affinity-optimized combinatorial variants of antibody specific to Eph receptor and/or Ephrin for treating cancer and inflammation)
IT 340830-03-7, Receptor tyrosine kinase
(class I-XIV and XVI-IX; affinity-optimized combinatorial variants of antibody specific to Eph receptor and/or Ephrin for treating cancer and inflammation)
IT 885234-88-8P 885234-89-9P
(nucleotide sequence; affinity-optimized combinatorial variants of antibody specific to Eph receptor and/or Ephrin for treating cancer and inflammation)
IT 813408-64-9, GenBank AJ872185 885234-15-1 885234-17-3 885234-19-5
885234-21-9 885234-23-1 885234-25-3 885234-27-5 885234-29-7

885234-31-1 885234-33-3 885234-35-5 885234-37-7 885234-39-9
885234-41-3 885234-43-5 885234-44-6 885234-47-9, DNA (Human Ephrin A1 variant 1 cDNA) 885234-49-1, DNA (Human Ephrin A1 variant 2 cDNA) 885234-51-5, DNA (Human Ephrin A2 cDNA) 885234-53-7, DNA (Human Ephrin A3 cDNA) 885234-55-9, DNA (Human Ephrin A 4 variant 1 cDNA) 885234-57-1, DNA (Human Ephrin A4 variant 2 cDNA) 885234-59-3, DNA (Human Ephrin A4 variant 3 cDNA) 885234-61-7, DNA (Human Ephrin A5 cDNA) 885234-63-9, DNA (Human Ephrin B1 cDNA) 885234-65-1, DNA (Human Ephrin B2 cDNA) 885234-67-3, DNA (Human Ephrin B3 cDNA) 885234-69-5
(nucleotide sequence; affinity-optimized combinatorial variants of antibody specific to Eph receptor and/or Ephrin for treating cancer and inflammation)

IT 127464-60-2, VEGF
(production inhibition; affinity-optimized combinatorial variants of antibody specific to Eph receptor and/or Ephrin for treating cancer and inflammation)

IT 885241-37-2
(unclaimed protein sequence; affinity-optimized combinatorial variants of antibody specific to Eph receptor and/or Ephrin for treating cancer and inflammation)

IT 95088-49-6 113516-56-6 113846-65-4 113846-66-5 122024-47-9
130838-28-7 132328-28-0 135702-75-9 137235-69-9 154511-01-0
154511-02-1 154511-04-3 154511-05-4 154511-06-5 154511-07-6
154511-08-7 154511-09-8 154511-10-1 154511-11-2 154511-12-3
154561-14-5 155547-57-2 160918-30-9 174490-42-7 185047-03-4
200405-35-2 206748-57-4 220540-59-0 244250-73-5 244283-56-5
261944-63-2 278595-84-9 285552-09-2 337489-94-8 447456-94-2
447456-95-3 455901-21-0 455901-22-1 455901-23-2 516484-43-8
604797-13-9 604797-14-0 604797-15-1 604797-16-2 604797-17-3
604797-18-4 604797-19-5 604797-20-8 615266-60-9 615266-61-0
828936-05-6 828936-06-7 828936-07-8 841262-88-2 841262-89-3
841262-90-6 850464-78-7 850464-79-8 850464-80-1 885127-27-5
885127-28-6 885127-29-7 885127-30-0 885127-31-1 885127-32-2
885127-33-3 885127-34-4 885127-35-5 885127-36-6 885127-37-7
885127-38-8
(unclaimed sequence; affinity-optimized combinatorial variants of antibody specific to Eph receptor and/or Ephrin for treating cancer and inflammation)

L15 ANSWER 53 OF 55 USPATFULL on STN

ACCESSION NUMBER: 2004:240296 USPATFULL

TITLE: Therapeutic agents useful for treating pain

INVENTOR(S): Sun, Qun, Princeton, NJ, UNITED STATES
Tafesse, Laykea, Robinsville, NJ, UNITED STATES
Victory, Sam, Newtown, PA, UNITED STATES

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2004186111	A1	20040923	
APPLICATION INFO.:	US 2003-739190	A1	20031219	(10)

	NUMBER	DATE	
PRIORITY INFORMATION:	US 2002-435917P	20021224	(60)
	US 2003-459626P	20030403	(60)
	US 2003-473856P	20030529	(60)

DOCUMENT TYPE: Utility

FILE SEGMENT: APPLICATION

LEGAL REPRESENTATIVE: JONES DAY, 51 Louisiana Aveue, N.W, WASHINGTON, DC, 20001-2113

NUMBER OF CLAIMS: 156

EXEMPLARY CLAIM: 1

LINE COUNT: 24955

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A compound of formula: ##STR1##

wherein Ar.sub.1, A, R.sub.3, x, and m are as disclosed herein and Ar.sub.2 is a benzothiazolyl, benzooxazolyl, or benzoimidazolyl group or a pharmaceutically acceptable salt thereof (a "Benzoazolylpiperazine Compound"), compositions comprising a Benzoazolylpiperazine Compound, and methods for treating or preventing pain, UI, an ulcer, IBD, IBS, an addictive disorder, Parkinson's disease, parkinsonism, anxiety, epilepsy, stroke, a seizure, a pruritic condition, psychosis, a cognitive disorder, a memory deficit, restricted brain function, Huntington's chorea, amyotrophic lateral sclerosis, dementia, retinopathy, a muscle spasm, a migraine, vomiting, dyskinesia, or depression in an animal comprising administering to an animal in need thereof an effective amount of a Benzoazolylpiperazine Compound are disclosed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT Nervous system, disease
(Huntington's chorea, treatment; preparation of (heterocyclylpiperazinyl)benzothiazoles, benzimidazoles, and benzooxazoles as metabotropic glutamate receptor antagonists and as ligands for VR1 in treatment of disorders such as addiction and pain)

IT Nervous system, disease
(amyotrophic lateral sclerosis, treatment; preparation of (heterocyclylpiperazinyl)benzothiazoles, benzimidazoles, and benzooxazoles as metabotropic glutamate receptor antagonists and as ligands for VR1 in treatment of disorders such as addiction and pain)

IT Mental disorder
(cognitive, treatment; preparation of (heterocyclylpiperazinyl)benzothiazoles, benzimidazoles, and benzooxazoles as metabotropic glutamate receptor antagonists and as ligands for VR1 in treatment of disorders such as addiction and pain)

IT Mental disorder
(depression, treatment; preparation of (heterocyclylpiperazinyl)benzothiazoles, benzimidazoles, and benzooxazoles as metabotropic glutamate receptor antagonists and as ligands for VR1 in treatment of disorders such as addiction and pain)

IT Cognition
(disorder, treatment; preparation of (heterocyclylpiperazinyl)benzothiazoles, benzimidazoles, and benzooxazoles as metabotropic glutamate receptor antagonists and as ligands for VR1 in treatment of disorders such as addiction and pain)

IT Nervous system, disease
(dyskinesia, treatment; preparation of (heterocyclylpiperazinyl)benzothiazoles, benzimidazoles, and benzooxazoles as metabotropic glutamate receptor antagonists and as ligands for VR1 in treatment of disorders such as addiction and pain)

IT Bladder, disease
(incontinence, treatment; preparation of (heterocyclylpiperazinyl)benzothiazoles, benzimidazoles, and benzooxazoles as metabotropic glutamate receptor antagonists and as ligands for VR1 in treatment of disorders such as addiction and pain)

IT Intestine, disease
(inflammatory, treatment; preparation of (heterocyclylpiperazinyl)benzothiazoles, benzimidazoles, and benzooxazoles as metabotropic glutamate receptor antagonists and as ligands for VR1 in treatment of disorders such as addiction and pain)

IT Intestine, disease
(irritable bowel syndrome, treatment; preparation of (heterocyclylpiperazinyl)benzothiazoles, benzimidazoles, and benzooxazoles as metabotropic glutamate receptor antagonists and as ligands for VR1 in treatment of disorders such as addiction and pain)

IT Glutamate receptors
(metabotropic, mGluR1; preparation of (heterocyclylpiperazinyl)benzothiazole s, benzimidazoles, and benzooxazoles as metabotropic glutamate receptor antagonists and as ligands for VR1 in treatment of disorders such as addiction and pain)
IT Glutamate receptors
(metabotropic, mGluR5; preparation of (heterocyclylpiperazinyl)benzothiazole s, benzimidazoles, and benzooxazoles as metabotropic glutamate receptor antagonists and as ligands for VR1 in treatment of disorders such as addiction and pain)
IT Headache
(migraine, treatment; preparation of (heterocyclylpiperazinyl)benzothiazoles , benzimidazoles, and benzooxazoles as metabotropic glutamate receptor antagonists and as ligands for VR1 in treatment of disorders such as addiction and pain)
IT Analgesics
IT Anticonvulsants
IT Antidepressants
IT Antiemetics
IT Antimigraine agents
IT Antiparkinsonian agents
IT Antipsychotics
IT Antiulcer agents
IT Anxiolytics
IT Human
(preparation of (heterocyclylpiperazinyl)benzothiazoles, benzimidazoles, and benzooxazoles as metabotropic glutamate receptor antagonists and as ligands for VR1 in treatment of disorders such as addiction and pain)
IT Mental disorder
(psychosis, treatment; preparation of (heterocyclylpiperazinyl)benzothiazole s, benzimidazoles, and benzooxazoles as metabotropic glutamate receptor antagonists and as ligands for VR1 in treatment of disorders such as addiction and pain)
IT Memory, biological
(retention defect, treatment; preparation of (heterocyclylpiperazinyl)benzot hiazoles, benzimidazoles, and benzooxazoles as metabotropic glutamate receptor antagonists and as ligands for VR1 in treatment of disorders such as addiction and pain)
IT Eye, disease
(retinopathy, treatment; preparation of (heterocyclylpiperazinyl)benzothiazo les, benzimidazoles, and benzooxazoles as metabotropic glutamate receptor antagonists and as ligands for VR1 in treatment of disorders such as addiction and pain)
IT Muscle, disease
(spasm, treatment; preparation of (heterocyclylpiperazinyl)benzothiazoles, benzimidazoles, and benzooxazoles as metabotropic glutamate receptor antagonists and as ligands for VR1 in treatment of disorders such as addiction and pain)
IT Muscle relaxants
(spasmolytics; preparation of (heterocyclylpiperazinyl)benzothiazoles, benzimidazoles, and benzooxazoles as metabotropic glutamate receptor antagonists and as ligands for VR1 in treatment of disorders such as addiction and pain)
IT Brain, disease
(stroke, treatment; preparation of (heterocyclylpiperazinyl)benzothiazoles, benzimidazoles, and benzooxazoles as metabotropic glutamate receptor antagonists and as ligands for VR1 in treatment of disorders such as addiction and pain)
IT Anxiety
IT Drug dependence
IT Epilepsy
IT Pain
IT Parkinson's disease

IT Pruritus
IT Seizures
IT Ulcer
IT Vomiting
(treatment; preparation of (heterocyclylpiperazinyl)benzothiazoles, benzimidazoles, and benzooxazoles as metabotropic glutamate receptor antagonists and as ligands for VR1 in treatment of disorders such as addiction and pain)

IT 722497-50-9P 722497-51-0P 722497-52-1P 722497-53-2P 722497-54-3P
722497-55-4P 722497-56-5P 722497-57-6P 722497-58-7P 722497-59-8P
722497-60-1P 722497-61-2P 722497-62-3P 722497-63-4P 722497-64-5P
722497-65-6P 722497-66-7P 722497-67-8P 722497-68-9P 722497-69-0P
722497-71-4P 722497-73-6P 722497-75-8P 722497-76-9P 722497-78-1P
722497-80-5P 722497-81-6P 722497-83-8P 722497-85-0P 722497-86-1P
722497-87-2P 722497-88-3P 722497-89-4P 722497-90-7P 722497-91-8P
722497-92-9P 722497-93-0P 722497-94-1P 722497-95-2P 722497-96-3P
722497-97-4P 722497-98-5P 722497-99-6P 722498-00-2P 722498-01-3P
722498-02-4P 722498-03-5P 722498-04-6P 722498-05-7P 722498-06-8P
722498-09-1P 722498-10-4P 722498-11-5P 722498-12-6P 722498-13-7P
722498-14-8P 722498-15-9P 722498-16-0P 722498-17-1P 722498-18-2P
722498-19-3P 722498-23-9P
(drug candidate; preparation of (heterocyclylpiperazinyl)benzothiazoles, benzimidazoles, and benzooxazoles as metabotropic glutamate receptor antagonists and as ligands for VR1 in treatment of disorders such as addiction and pain)

IT 664379-55-9, VR1
(preparation of (heterocyclylpiperazinyl)benzothiazoles, benzimidazoles, and benzooxazoles as metabotropic glutamate receptor antagonists and as ligands for VR1 in treatment of disorders such as addiction and pain)

IT 94-45-1, 6-Ethoxy-2-benzothiazolamine 95-24-9, 6-Chloro-2-benzothiazolamine 110-85-0, Piperazine, reactions 136-95-8, 2-Benzothiazolamine 348-40-3 777-12-8 2402-77-9, 2,3-Dichloropyridine 2536-91-6, 6-Methyl-2-benzothiazolamine 4858-85-9, 2,3-Dichloropyrazine 4887-95-0 5728-20-1, 4,5-Dichloro-2,1,3-thiadiazole 15864-32-1, 6-Bromo-2-benzothiazolamine 15965-54-5 18368-76-8, 2-Chloro-3-methylpyridine 19064-64-3 32895-14-0 39791-96-3 39791-97-4 53146-48-8 60434-99-3 65753-47-1, 2-Chloro-3-(trifluoromethyl)pyridine 74879-18-8, (S)-2-Methylpiperazine 75336-86-6, (R)-2-Methylpiperazine 131395-10-3 393513-95-6 683240-69-9 722498-20-6 722498-21-7
(starting material; preparation of (heterocyclylpiperazinyl)benzothiazoles, benzimidazoles, and benzooxazoles as metabotropic glutamate receptor antagonists and as ligands for VR1 in treatment of disorders such as addiction and pain)

L15 ANSWER 54 OF 55 USPATFULL on STN
ACCESSION NUMBER: 2006:61268 USPATFULL
TITLE: Bioactive compounds and methods of uses thereof
INVENTOR(S): Ho, Chi-Tang, East Brunswick, NJ, UNITED STATES
Bai, Naisheng, Highland Park, NJ, UNITED STATES
Dong, Zigang, Rochester, MN, UNITED STATES
Bode, Ann M., Cannon Falls, MN, UNITED STATES
Dushenkov, Slavik, Fort Lee, NJ, UNITED STATES

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2006052438	A1	20060309	
APPLICATION INFO.:	US 2005-118915	A1	20050429	(11)

	NUMBER	DATE	
PRIORITY INFORMATION:	US 2004-567340P	20040430	(60)

DOCUMENT TYPE: Utility

FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: JONES DAY, 222 EAST 41ST ST, NEW YORK, NY, 10017, US
NUMBER OF CLAIMS: 24
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 15 Drawing Page(s)
LINE COUNT: 5420
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB In one aspect, the present invention provides compounds having formula I or IV as shown below: ##STR1## as further defined herein. In additional aspects, the present invention provides compositions and kits comprising the compounds of the invention and methods for their use, for example, for the prevention or treatment of a cancer.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT Anti-infective agents
IT Anti-inflammatory agents
IT Antitumor agents
IT Cosmetics
IT Extraction
IT Food additives
IT Human
IT Infection
IT Inflammation
IT Neoplasm
IT Rabdosia rubescens
(bioactive compds. such as depsides and diterpenoids and methods of uses thereof for treatment of diseases such as cancer in relation to isolation from Rabdosia rubescens)
IT Drug delivery systems
(carriers; bioactive compds. such as depsides and diterpenoids and methods of uses thereof for treatment of diseases such as cancer in relation to isolation from Rabdosia rubescens)
IT Polyamides, biological studies
(compds. purification by; bioactive compds. such as depsides and diterpenoids and methods of uses thereof for treatment of diseases such as cancer in relation to isolation from Rabdosia rubescens)
IT Drug delivery systems
(diluents; bioactive compds. such as depsides and diterpenoids and methods of uses thereof for treatment of diseases such as cancer in relation to isolation from Rabdosia rubescens)
IT Drug delivery systems
(excipients; bioactive compds. such as depsides and diterpenoids and methods of uses thereof for treatment of diseases such as cancer in relation to isolation from Rabdosia rubescens)
IT Diet
(supplements; bioactive compds. such as depsides and diterpenoids and methods of uses thereof for treatment of diseases such as cancer in relation to isolation from Rabdosia rubescens)
IT Drug delivery systems
(vehicles; bioactive compds. such as depsides and diterpenoids and methods of uses thereof for treatment of diseases such as cancer in relation to isolation from Rabdosia rubescens)
IT 128887-80-9P, Rabdoternin A 128887-81-0P, Rabdoternin B 155969-81-6P, Rubescensin M 664306-56-3P 878049-61-7P, Rubscendepside 878049-62-8P, Rubescensin J 878049-63-9P 878049-64-0P
(bioactive compds. such as depsides and diterpenoids and methods of uses thereof for treatment of diseases such as cancer in relation to isolation from Rabdosia rubescens)
IT 64-17-5, Ethanol, biological studies 67-56-1, Methanol, biological studies
(compds. elution with; bioactive compds. such as depsides and diterpenoids and methods of uses thereof for treatment of diseases such as cancer in relation to isolation from Rabdosia rubescens)

IT 9003-70-7, Divinylbenzene-styrene copolymer
(resins, compds. purification by; bioactive compds. such as depsides and diterpenoids and methods of uses thereof for treatment of diseases such as cancer in relation to isolation from Rabdosia rubescens)

L15 ANSWER 55 OF 55 USPATFULL on STN

ACCESSION NUMBER:	2004:166011 USPATFULL		
TITLE:	Therapeutic agents useful for treating pain		
INVENTOR(S):	Chen, Zhengming, Belle Mead, NJ, UNITED STATES Tafesse, Laykea, Robbinsville, NJ, UNITED STATES		
	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2004127501	A1	20040701
APPLICATION INFO.:	US 2003-669875	A1	20030923 (10)
	NUMBER		DATE
PRIORITY INFORMATION:	US 2002-413193P		20020924 (60)
	US 2003-456042P		20030319 (60)
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	APPLICATION		
LEGAL REPRESENTATIVE:	JONES DAY, 222 EAST 41ST ST, NEW YORK, NY, 10017		
NUMBER OF CLAIMS:	54		
EXEMPLARY CLAIM:	1		
LINE COUNT:	8534		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention provides a compound of formula: ##STR1##

(where R.sub.1, R.sub.2, R.sub.3, A, n, and p are disclosed herein) or a pharmaceutically acceptable salt thereof (a "2-Pyrimidinylpiperazine Compound"); pharmaceutical compositions comprising an effective amount of a 2-Pyrimidinylpiperazine Compound; and methods for treating or preventing a condition such as pain, urinary incontinence, an addictive disorder, Parkinson's disease, parkinsonism, anxiety, epilepsy, stroke, a seizure, a pruritic condition, psychosis, a cognitive disorder, a memory deficit, restricted brain function, Huntington's chorea, amyotrophic lateral sclerosis, dementia, retinopathy, a muscle spasm, a migraine, vomiting, dyskinesia, or depression in an animal comprising administering to an animal in need thereof an effective amount of a 2-Pyrimidinylpiperazine Compound.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT Glutamate receptors
(metabotropic, mGluR5, antagonists; preparation of alkynylpiperazinylpyrimidines as mGluR5 receptor function inhibitors for treatment of pain, addiction, Parkinson's disease, etc.)
IT Analgesics
IT Antiparkinsonian agents
IT Antipsychotics
IT Anxiolytics
IT Drug delivery systems
IT Human
(preparation of alkynylpiperazinylpyrimidines as mGluR5 receptor function inhibitors for treatment of pain, addiction, Parkinson's disease, etc.)
IT Anxiety
IT Drug dependence
IT Pain
IT Parkinson's disease
IT Schizophrenia
(treatment; preparation of alkynylpiperazinylpyrimidines as mGluR5 receptor function inhibitors for treatment of pain, addiction, Parkinson's disease, etc.)

IT 676596-25-1P 676596-26-2P 676596-27-3P 676596-28-4P 676596-29-5P
676596-30-8P 676596-31-9P 676596-32-0P 676596-33-1P 676596-34-2P
676596-35-3P
(preparation of alkynylpiperazinylpyrimidines as mGluR5 receptor function inhibitors for treatment of pain, addiction, Parkinson's disease, etc.)

IT 109-07-9, 2-Methylpiperazine 110-85-0, Piperazine, reactions
352-34-1, 1-Fluoro-4-iodobenzene 471-25-0, Propiolic acid 637-44-5,
3-Phenyl-2-propynoic acid 1120-90-7, 3-Iodopyridine 1722-12-9,
2-Chloropyrimidine 2579-22-8, 3-Phenyl-2-propynal 4472-44-0,
2-Chloro-4,6-dimethylpyrimidine 5029-67-4, 2-Iodopyridine 5424-21-5,
2,6-Dichloro-4-methylpyrimidine 20980-22-7, 1-(2-Pyrimidinyl)piperazine
22536-64-7, 2-Chloro-4-methyl-6-methoxypyrimidine 33034-67-2,
2-Chloro-4-trifluoromethylpyrimidine 57260-71-6 94021-22-4,
1-(2-Pyrimidinyl)piperazine dihydrochloride 171197-80-1,
2-Fluoro-5-iodopyridine
(preparation of alkynylpiperazinylpyrimidines as mGluR5 receptor function inhibitors for treatment of pain, addiction, Parkinson's disease, etc.)

IT 22746-09-4P 59215-34-8P 179756-91-3P 676596-36-4P 676596-37-5P
676596-38-6P
(preparation of alkynylpiperazinylpyrimidines as mGluR5 receptor function inhibitors for treatment of pain, addiction, Parkinson's disease, etc.)

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Volume 6, No 4 June 2003

The impact of LH serum concentration on the clinical outcome of IVF cycles in patients receiving two regimens of clomiphene citrate/gonadotrophin/0.25 mg cetrorelix

A Tavaniotou[1], C Albano[1], A Van Steirteghem[1], P Devroey[2,3]
[1]Centre for Reproductive Medicine, Dutch-Speaking Free University of Brussels, Brussels, Belgium
[2]AZ-VUB, Centre for Reproductive Medicine, Laarbeeklaan 101, B-1090 Brussels, Belgium
[3]Correspondence: email: paul.devroey@az.vub.ac.be

Clomiphene citrate treatment with the association of gonadotrophins and the GnRH antagonist cetrorelix 0.25mg was analysed in two different stimulation protocols for IVF. In protocol I, 18 patients were sequentially stimulated with clomiphene citrate and gonadotrophins. In protocol II, 28 patients started the gonadotrophin injections during the clomiphene citrate administration. LH values significantly dropped after the first 0.25 mg cetrorelix injection in both protocols. A total of 22% and 7% of cycles were cancelled in protocols I and II, respectively, because of poor follicular development. The clinical pregnancy rate following embryo transfer was 16.1% in protocol I and 29.1% in protocol II. In two (11.1%) cycles stimulated according to protocol I and in eight (28.5%) cycles from protocol II, premature LH surges occurred. In patients with premature LH surge, significantly fewer metaphase II oocytes were obtained. The clinical pregnancy rate following embryo transfer was 12.5% in patients with surge compared with 29.5% in patients without. LH values were lower before oocyte retrieval in patients who achieved pregnancy in the study cycle. In conclusion, sequential clomiphene citrate and gonadotrophin administration is not recommended for clomiphene citrate/gonadotrophin/cetrorelix 0.25 cycles. Cetrorelix 0.25 mg/day was associated with a high incidence of premature LH surges and premature LH surges were associated with an adverse cycle outcome.

Reproductive BioMedicine Online 2003 Vol. 6, No. 4, 421–426

Keywords: Cetrorelix, clomiphene citrate, GnRH antagonist, in vitro fertilization, luteinizing hormone

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Previous miscarriages influence IVF and intracytoplasmic sperm injection pregnancy outcome